

1           IN THE UNITED STATES DISTRICT COURT  
2           FOR THE NORTHERN DISTRICT OF OHIO  
3           EASTERN DIVISION

- - -

4           IN RE: NATIONAL                   : HON. DAN A.  
5           PRESCRIPTION OPIATE           : POLSTER  
6           LITIGATION                    :  
7   :  
8           APPLIES TO ALL CASES           : NO.  
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- HIGHLY CONFIDENTIAL -

SUBJECT TO FURTHER CONFIDENTIALITY REVIEW

VOLUME II

- - -

November 14, 2018

- - -

15                   Videotaped deposition of  
16           BRUCE L. MOSKOVITZ, M.D., taken pursuant  
17           to notice, was held at the law offices of  
18           Drinker Biddle & Reath, 105 College Road  
19           East, Princeton, New Jersey, beginning at  
20           9:17 a.m., on the above date, before  
21           Michelle L. Gray, a Registered  
22           Professional Reporter, Certified  
23           Shorthand Reporter, Certified Realtime  
24           Reporter, and Notary Public.

- - -

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I N D E X  
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Testimony of:

BRUCE L. MOSKOVITZ, M.D.

By Ms. Conroy 339, 691, 753, 760

By Mr. Lifland 534, 746, 758

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None.

Request for Production of Documents

PAGE LINE

None.

Stipulations

PAGE LINE

None.

Questions Marked

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None.

1

- - -

2

THE VIDEOGRAPHER: We are

3

back on the record. Today's date

4

is November 14th, 2018. And the

5

time is 9:17 a.m.

6

Counsel, you may proceed.

7

- - -

8

... BRUCE L. MOSKOVITZ, M.D.,

9

having been previously sworn, was

10

examined and testified as follows:

11

- - -

12

CONTINUED EXAMINATION

13

- - -

14

BY MS. CONROY:

15

Q. Good morning, Doctor.

16

A. Good morning.

17

Q. Thank you for bringing the

18

sun back.

19

A. We don't often get it in New

20

Jersey at this time of year.

21

Q. Right. I guess we're

22

avoiding a snowstorm for a few more hours

23

I guess. What I'd like to talk about

24

first this morning is the reservoir patch

1       versus the matrix patch. And let's see.  
2       I think maybe one way to address it at  
3       first is what I've marked as Exhibit 20.

4                       (Document marked for  
5                       identification as Exhibit  
6                       Janssen-Moskovitz-20.)

7       BY MS. CONROY:

8               Q.       This is an e-mail from  
9       you -- this is an e-mail from you to Drew  
10       Jones at ALZA. Is that --

11              A.       ALZA.

12              Q.       ALZA? And who is Drew  
13       Jones.

14              A.       I believe he was the  
15       physician in the R&D area at ALZA. They  
16       were the original manufacturing of  
17       Duragesic.

18              Q.       And is GV Gary Vorsanger?

19              A.       I'm sorry. Are you  
20       seeing --

21              Q.       On the cc.

22              A.       I would assume so.

23                      MR. LIFLAND: Are we reading  
24       the Bates numbers into the record

1                   for the exhibits?

2                   MS. CONROY: I'm happy to if  
3                   you want the Bates number.

4                   It's JAN-MS-01196284, and  
5                   it's Exhibit 20.

6                   MR. LIFLAND: Thank you.

7 BY MS. CONROY:

8                   Q. And I see that your  
9                   signature line, it says, "Executive  
10                  director, primary care."

11                  A. Yes.

12                  Q. Is that, we saw yesterday  
13                  pain/mycology. Did the department name  
14                  change or --

15                  A. I can only answer that by  
16                  saying over the course of time in medical  
17                  affairs, there were a variety of marketed  
18                  products that fell under my  
19                  responsibility. And so certainly by  
20                  2003, there was no longer a focus on the  
21                  anti-fungals.

22                  So while the core  
23                  responsibilities for marketed products  
24                  remained the same, the title may have

1 changed periodically.

2 Q. Was it considered primary  
3 care instead of pain, do you know?

4 A. There was a period of time  
5 when Janssen itself changed its name to  
6 Pri-Cara, which reflected our focus on  
7 primary care. So the change in title may  
8 have been related to the change in the  
9 focus even at the company level. And  
10 then subsequently it became Janssen  
11 Ortho-McNeil, and after that Janssen.

12 Q. Okay. Take a look at  
13 Dr. Jones' e-mail to you, which is at the  
14 bottom which was earlier in the day to  
15 you. Think the folks in Europe will have  
16 some issues with studies which might  
17 generate data suggesting matrix is a more  
18 abusable product than form-filled  
19 Duragesic."

20 Do you see that?

21 A. Yes, I do.

22 Q. Can you describe for me in  
23 this e-mail if you know what is meant by  
24 matrix?

1           A.       Yes. We were aware at this  
2       period of time, 2003, that there was  
3       another company that was developing a  
4       formulation of the Duragesic patch in  
5       which fentanyl would be delivered, not  
6       through a reservoir but through what we  
7       term a "matrix," which is a solid fill.  
8       It's fentanyl in a solid fill  
9       formulation. And -- so we knew that they  
10      would be coming out with that in the  
11      United States.

12                    There was a matrix  
13      formulation already available marketed by  
14      Janssen in Europe.

15           Q.       Was that a similar  
16      formulation, the one that Janssen  
17      marketed in Europe?

18           A.       Well, if by similar you mean  
19      pharmacokinetically did it deliver the --  
20      the same controlled rate of fentanyl,  
21      yes.

22           Q.       I thank -- thank you for  
23      that. What I'm talking about more is,  
24      was it considered a matrix patch?

1 A. Yes, it was.

2 Q. Okay. So -- so Janssen had  
3 a matrix patch in Europe --

4 A. Yes.

5 Q. -- that it was selling?

6 A. Yes.

7 Q. And in the U.S., what kind  
8 of a patch was Janssen selling at that  
9 time?

10 A. It was still the form-filled  
11 patch. It was still a reservoir in which  
12 the fentanyl is between two layers as a  
13 semi liquid in an alcohol base in hydroxy  
14 cellulose I believe.

15 Q. Okay. Was Janssen selling a  
16 matrix patch of any sort in the U.S. at  
17 this time in 2003?

18 A. No.

19 Q. At some point they did  
20 switch to the -- to the matrix patch?

21 A. Yes.

22 Q. Okay. Approximately what  
23 year did they switch?

24 A. I believe that was in 2007,

1 approval 2008.

2 MR. LIFLAND: If you -- you  
3 should -- you do have the -- the  
4 timeline if you want to --

5 THE WITNESS: Yeah, so let  
6 me go back to that. I'm sorry.

7 Yeah, it was in --

8 BY MS. CONROY:

9 Q. We're going to -- we're  
10 going to look at some documents, but  
11 you're -- I'm happy to have you look at  
12 this time --

13 A. Yeah, so it was in 2009 that  
14 we marketed. The -- the data to develop  
15 the pharmacokinetic information was  
16 developed earlier.

17 Q. Okay. Now, if you take a  
18 look at your response to Dr. Jones, you  
19 say, "Bingo. It's why it's so important  
20 to touch base with all stakeholders."

21 What do you mean by  
22 stakeholders?

23 A. So anything that happens in  
24 any one country is shared with all the

1 regulatory authorities in all the other  
2 countries. And so we never want to do  
3 something in a void where we're not  
4 informing our subsidiaries and -- and  
5 other countries where products would be  
6 marketed of what's going on in our  
7 country, because there would be concerns  
8 in -- in another country over what might  
9 be happening in the first -- in the first  
10 country.

11 Q. And that's because you,  
12 Janssen in the United States, was looking  
13 at conducting some tests that would not  
14 have been advantageous to the matrix  
15 patch that Duragesic Janssen was selling  
16 in -- in Europe?

17 A. I -- I wouldn't characterize  
18 it that way. We were looking at whether  
19 there would be differences in issue -- we  
20 didn't know ahead of time, otherwise we  
21 wouldn't be conducting the studies, but  
22 we had concerns based upon an earlier  
23 report that there may be different issues  
24 around abuse, misuse, diversion, in the

1 United States between a reservoir patch  
2 and a matrix patch.

3 Q. Different issues between the  
4 United States and Europe?

5 A. Well, that's one of the  
6 things that we explored.

7 Q. And what was -- what was  
8 your conclusion?

9 A. Well, so there are a couple  
10 of components to that. I mean we  
11 ultimately did do studies that suggested  
12 to us that in the United States there may  
13 be differences in attractiveness of -- of  
14 a matrix patch compared with a reservoir  
15 patch in potential for abuse, misuse and  
16 diversion.

17 At the same time,  
18 recognizing that there was a matrix patch  
19 in Europe, we commissioned an expert  
20 report on the part of a German expert in  
21 pain management to assess whether the  
22 same concerns that we explored in the  
23 United States were valid for Europe. And  
24 it was his conclusion that the

1 environment around abuse, misuse and  
2 diversion in the United States,  
3 particularly access to other drugs,  
4 differed between the United States and  
5 Europe such that the -- the concerns we  
6 had about bringing a matrix patch to the  
7 market in the United States were  
8 different for Europe. And the same  
9 issues would not lead to the levels of  
10 concern for abuse, misuse and diversion  
11 in Europe.

12 Q. When -- when approximately  
13 did you -- I take it Janssen consulted  
14 and hired the German expert?

15 A. Yes.

16 Q. Approximately when was that?

17 A. 2003, 2004. I believe the  
18 report came out in 2004.

19 Q. And was that a report to  
20 you?

21 A. It was a report to -- well,  
22 I -- I certainly received the report.  
23 I -- I don't recall exactly who the  
24 report was directed to.

1           Q.     Did you -- were you the  
2     person who requested the report of the  
3     German expert?

4           A.     No. That was -- I believe  
5     the report -- I can't say for certain, I  
6     believe the report was requested by the  
7     head of the pain group, the worldwide  
8     pain group on the R&D side.

9           Q.     Do you remember the expert's  
10    name?

11          A.     It was a German name,  
12    Juergen Haeussler, I believe, was the one  
13    who requested it. He may have requested  
14    it from his PGSM counterparts. But I  
15    believe Juergen Haeussler was the one who  
16    requested that -- that report.

17          Q.     He was -- as best you can  
18    recall, he was head of worldwide pain at  
19    R and -- R&D?

20          A.     At the R -- on the R&D side.

21          Q.     Do you remember the name of  
22    the actual expert?

23          A.     No, I don't.

24          Q.     Or do you know where the

1 expert practiced, I mean what hospital --

2 A. I believe it was in Germany.

3 Q. Was it a man or a woman, do  
4 you know?

5 A. It was a gentleman.

6 Q. And do you recall today what  
7 environmental -- what environmental  
8 differences there were between the United  
9 States and Germany with respect to abuse  
10 and diversion of matrix patches?

11 A. I'd have to go back and  
12 refer to the actual report. But my best  
13 recollection was that there were -- there  
14 was access to other compounds, including  
15 heroin in -- in Europe such that the fact  
16 that a matrix formulation of fentanyl was  
17 available was not going to be a driver  
18 of -- of a switch to fentanyl from other  
19 compounds that were widely available, and  
20 access to other compounds in Europe  
21 compared with the United States.

22 Q. Licit or illicit compounds?

23 A. Both licit and illicit.

24 Q. Was it the finding of the

1 German expert that there was more access  
2 to heroin in Germany than in the United  
3 States?

4 A. I believe that was part of  
5 the report.

6 Q. Have you seen that report  
7 recently?

8 A. No, I have not.

9 Q. It wasn't something that you  
10 reviewed in advance of your -- either  
11 your 30(b)(6) deposition or this  
12 deposition?

13 A. If I did review it, it was  
14 quite some time ago. So I don't have a  
15 recent recollection of it.

16 Q. Do you recall what -- did  
17 you review it in advance of your Oklahoma  
18 deposition?

19 A. Same answer. In a -- in a  
20 general sense I reviewed documents around  
21 what became the Citizen's Petition and  
22 that was part of the research that was  
23 done into differences between the United  
24 States and Europe. But I don't recall

1       whether I reviewed that specific document  
2       or simply had a recollection of it from  
3       the time that I was at Janssen.

4               Q.       Okay. "PGSM," the  
5       pharmaceutical group strategic --

6               A.       Management --

7               Q.       -- management "should be  
8       able to weigh in with the EU concerns."

9               So this was before they  
10       actually had the German report, correct?

11              A.       I believe so.

12              Q.       "It may very well be that  
13       abuse issues are different in Europe, but  
14       at the end of the day, the U.S. has a  
15       \$1.2 billion at stake."

16              What were you -- what's the  
17       \$1.2 billion at stake, what were you  
18       referring to?

19              A.       I believe I was referring to  
20       sales of Duragesic in the United States.

21              Q.       And how did you know the  
22       numbers of -- for the sales of Duragesic  
23       in the U.S.?

24              A.       It was probably available to

1 me through the sales and marketing group.

2 Q. "If the Duragesic  
3 reservoir" -- that's the reservoir  
4 matrix -- I mean the reservoir patch?

5 A. Yes.

6 Q. "If the reservoir is less  
7 abusable than an unprotected matrix  
8 patch, we need to get that message out  
9 with credible data to back it up."

10 What do you mean by  
11 "unprotected matrix patch"?

12 A. I believe this referred to  
13 the fact that Duragesic reservoir had a  
14 rate limiting membrane as part of the  
15 system; whereas, it was our understanding  
16 that the matrix patch, particularly the  
17 matrix patch that we anticipated coming  
18 to market in the United States, did not  
19 have a rate limiting membrane.

20 Q. And you say, "We need to get  
21 that message out with credible data to  
22 back it up." We talked yesterday about  
23 basically one of your responsibilities  
24 at -- in medical affairs to develop

1 clinical studies or clinical trials or  
2 whatever, to develop data that would show  
3 advantages or disadvantages with  
4 competing products. Is that what you're  
5 talking about here?

6 A. Yes. We would want to  
7 conduct studies that explored  
8 differences -- potential differences in  
9 abuse, misuse, and diversion between the  
10 marketed reservoir patch and a matrix  
11 patch.

12 Q. And at that time your  
13 working hypothesis, I take it, was that  
14 the reservoir was less abusable?

15 A. Well, at that time we  
16 already had a report in 2001. There was  
17 the Pinney report that we commissioned in  
18 2001 that had concluded that Janssen  
19 should not, in the United States, proceed  
20 with a switch to a matrix patch because  
21 there were concerns that a matrix patch  
22 could have a higher risk for abuse,  
23 misuse and diversion. And, therefore, we  
24 didn't switch in the United States.

1           Q.       Would it have been the same  
2       patch that was -- if you had switched, if  
3       you know, would it have been the same  
4       patch that was being sold in Europe?

5           A.       I assume so. I can't speak  
6       to the manufacturing side.

7           Q.       Okay. Do you know if the --  
8       well, the Janssen matrix patch had been  
9       approved by the FDA, even though I  
10      understand that you were not selling it  
11      in the U.S. at that time?

12          A.       In 2003?

13          Q.       Right.

14          A.       No.

15          Q.       It had not been?

16          A.       We had not submitted the  
17      data for approval.

18          Q.       Let me show you Exhibit 21.  
19                    (Document marked for  
20                    identification as Exhibit  
21                    Janssen-Moskovitz-21.)

22      BY MS. CONROY:

23          Q.       And this is  
24      JAN-MS-011196462.

1                   Exhibit 21 is a  
2     February 3rd, 2004, e-mail, at least the  
3     top, from you to Richard Allcorn. And  
4     you'll see at the bottom there is an  
5     e-mail from Dr. Allcorn to you. And  
6     attached to that is -- are some slides.  
7     Does that look like -- does that look  
8     like a printout of slides to you?

9                   A.     Yes.

10                  Q.     Okay. Who is Dr. Allcorn?

11                  A.     I don't know that he was a  
12     doctor. He was the head of the  
13     Mudskipper group that we spoke about  
14     yesterday, the group that we contracted  
15     with to put together the comprehensive  
16     summary of all the information that we  
17     developed from developing the reservoir  
18     patch to the matrix patch. And they  
19     ultimately put together a White Paper  
20     that summarized all that information.

21                  Q.     He signs his name "Dr." But  
22     you're not -- are you not sure?

23                  A.     It would not be an M.D. If  
24     he -- if he was -- if he signs his name

1 doctor, it's because he has a Ph.D., and  
2 I don't know in what.

3 Q. Okay. Where is he located?

4 A. In the UK.

5 Q. And have you ever met him  
6 face to face?

7 A. Yes, I have.

8 Q. And how did you know him?

9 A. I believe -- my best  
10 recollection is that Gary Vorsanger had  
11 worked with him with other projects and  
12 was impressed with his ability to  
13 synthesize the data into a readily  
14 accessible and readable format. And so  
15 after speaking with him and feeling  
16 comfortable that in fact they could do  
17 that, we brought them on.

18 Q. Now, so that I understand,  
19 Janssen would prepare, or generate the  
20 data and then Dr. Allcorn, Mudskipper,  
21 would write it up?

22 A. It's not that Janssen would  
23 generate the data. We would -- we  
24 ultimately funded a number of studies.

1 Some of them were internal. Some of them  
2 were external to Janssen, such as the  
3 attractiveness scale that Inflexxion did.  
4 So the data came from various sources.  
5 Ultimately all the data were fed into a  
6 summary document that reflected all the  
7 information we generated ourselves or  
8 through outside groups.

9 Q. And even -- so Dr. Allcorn's  
10 White Paper would have included only  
11 studies or data points that had either  
12 been generated by Janssen itself or by  
13 Janssen-sponsored investigators such as  
14 Inflexxion?

15 A. Yes. So if I may take a  
16 step back. This process started with an  
17 advisory group to look at a number of  
18 potential areas of research that would  
19 help to differentiate the reservoir patch  
20 from the matrix patch. Ultimately we  
21 embarked on funding a select group of  
22 those studies that could be done within a  
23 reasonable period of time.

24 And it was those studies

1     that were summarized in the White Paper  
2     report that Mudskipper put together for  
3     us, and that became the basis of the  
4     Citizen's Petition.

5             Q.     And I take it -- I take from  
6     what you just told me then that  
7     Dr. Allcorn did not -- was not going  
8     outside of Janssen or Janssen-sponsored  
9     studies to write his White Paper; he was  
10    using Janssen information?

11            A.     In terms of the data, yes.  
12    In terms of a backgrounder, he -- he  
13    would have included broadly available  
14    information about risks of abuse, misuse  
15    and diversion. But in terms of reporting  
16    the data, it was strictly what was  
17    provided to him.

18            Q.     And was he -- was he paid  
19    for that work, to write the paper?

20            A.     Yes. Well, Mudskipper was.

21            Q.     Mudskipper.

22                    And do you -- do you know  
23    whether there was a particular agreement  
24    that was signed with him? I think that

1     there's some -- I saw something, a  
2     reference to an agreement. But would  
3     that have been you, or would that have  
4     been a different department at Janssen  
5     that would have negotiated that agreement  
6     with him?

7             A.     It would have been a  
8     different department within Janssen. But  
9     yes, there was an agreement. I can't  
10    recall exactly who signed the formal  
11    agreement, but he would have been paid  
12    for the work that he did.

13            Q.     Did you meet face-to-face  
14    with anyone from Mudskipper to prepare  
15    this -- while they were preparing this  
16    White Paper?

17            A.     We had some face-to-face  
18    meetings and some teleconferences to  
19    discuss the formatting and where the data  
20    would be coming from. So yes.

21            Q.     If you take a look at your  
22    e-mail back to Dr. Allcorn. You tell him  
23    that apparently you're preparing -- there  
24    is going to be a teleconference on

1 Friday. And then you say, "I've attached  
2 slides that we've used to outline the  
3 abuse program we are embarking on."

4 We'll take a look at those  
5 slides in a minute.

6 But then if you go to the  
7 next paragraph, it says, "The focus of  
8 activities now is to differentiate  
9 Duragesic (reservoir) from the  
10 unprotected matrix patch."

11 So I think you've been  
12 telling me that was what you'd been  
13 planning to do. And now you're stating  
14 it; is that correct?

15 A. That's correct.

16 Q. You go on -- you say, "There  
17 are a series of studies we or ALZA will  
18 conduct, including attractiveness,  
19 concept mapping, Inflexxion." Those are  
20 the two companies that will perform those  
21 studies, correct, the attractiveness  
22 studies?

23 A. Yes.

24 Q. "Ease of extraction" --

1           A.       Well, it's not two  
2       companies. Concept mapping is the type  
3       of study, and it would be conducted by  
4       Inflexxion.

5           Q.       Thank you. And then ease of  
6       extraction also to be conducted by  
7       Inflexxion?

8           A.       Yes.

9           Q.       And PK, is that  
10      pharmacokinetics?

11          A.       Yes, it is.

12          Q.       -- "studies that are  
13      expected to show clinically relevant  
14      differences in serum concentrations under  
15      conditions likely to be encountered in  
16      clinical practice (we know the matrix  
17      patch is bioequivalent in 'normal healthy  
18      volunteers')."

19                   Can you explain to me what  
20      that means, what you were attempting to  
21      do with the serum concentration study?

22          A.       Yes. So before a generic  
23      compound could be approved or even a  
24      switch from reservoir to another

1 formulation, one of the regulatory  
2 requirements is to show that it's  
3 bioequivalent. That is to say that,  
4 depending upon the route of  
5 administration, in this case obviously it  
6 was transdermal, that the -- the amount  
7 of the active product, in this case,  
8 fentanyl, that enters the bloodstream  
9 over a period of time is similar within  
10 specified regulatory guidelines to the  
11 original compound.

12 So in this case, the matrix  
13 compound in a healthy normal patient --  
14 volunteer population, subject population,  
15 would have to show that the fentanyl  
16 transfer into the bloodstream was the  
17 same between the matrix patch and the  
18 reservoir patch within accepted  
19 regulatory guidelines for -- for  
20 determining bioequivalence.

21 Q. And did you -- was it your  
22 expectation in the studies that there  
23 would be differences between the  
24 reservoir and the matrix patch with

1     respect to the serum blood levels that  
2     would -- that would reach a patient?

3             A.     In other conditions outside  
4     of routine applying a patch to a normal  
5     healthy volunteer.

6             Q.     So give me an example of  
7     what that might be.

8             A.     So that might be -- if you  
9     look at the package insert, there are  
10    warnings against heat sources. So for  
11    patients who might have fever, for  
12    patients who might be exposed to heat  
13    sources such as heating pads or sauna,  
14    that in those situations there might be a  
15    difference in delivery of the fentanyl  
16    between a -- a reservoir patch that was  
17    sold in the United States and a  
18    hypothetical matrix patch.

19            Q.     Who would get more of the --  
20    of the drug?

21            A.     Well --

22            Q.     Under those -- under the  
23    conditions you're talking about, like  
24    heat?

1           A.       So ultimately we did show  
2       that under certain conditions -- and  
3       another condition also was denuded skin.

4           Q.       Would mean abraded --

5           A.       Abrade -- abraded --

6           Q.       -- or if someone had an  
7       open, some sort of open --

8           A.       A wound or even if they put  
9       a patch on the same area. The package  
10      insert warns against putting a patch  
11      on -- in the same area, but in situations  
12      like that, ultimately we did show that  
13      there were differences in delivery of  
14      fentanyl between the matrix and the  
15      reservoir patch.

16          Q.       And the difference that you  
17      showed was that the matrix patch could,  
18      under certain conditions, such as heat or  
19      abraded skin, deliver more fentanyl to a  
20      patient?

21          A.       Potentially, yes.

22          Q.       Then you go on and say, "A  
23      white paper will collect available data  
24      and new data as they are generated to

1 'paint' a full picture of risks  
2 associated with the matrix patch."

3 So this was an attempt to  
4 differentiate between the reservoir patch  
5 as a safer patch than the matrix patch?

6 A. Well, let's be careful on  
7 the term "safe." We were looking  
8 specifically at issues of abuse, misuse,  
9 diversion. Safety encompasses a lot more  
10 than that, including adverse event  
11 profile.

12 So we were looking at  
13 primarily issues of abuse, misuse and  
14 diversion. And our hypothesis in doing  
15 the studies was that there may be  
16 differences in those areas between the  
17 reservoir patch and the matrix patch.

18 Q. Would you agree with me,  
19 however, that heat conditions in abraded  
20 skin, that would be -- that's not abuse,  
21 diversion or misuse?

22 A. Well, in a sense it's -- if  
23 you -- if you apply heat, you are  
24 misusing the patch.

1           Q.       What about someone who is in  
2       a sauna, is that a misuse of the patch?

3           A.       In the sense that the  
4       package insert warns against exposing the  
5       patch to a heat source including sauna,  
6       it would be misusing the patch.

7           Q.       Does it say sauna in the  
8       label?

9           A.       It does.

10          Q.       And what about in a warm  
11       car, something like that, did you test it  
12       in conditions where it wasn't something  
13       like a sauna, but where you were in an  
14       environment that was very warm?

15          A.       I think in a broad sense we  
16       warn against heat sources, and examples  
17       of the heat sources might be a heating  
18       pad or a sauna or a fever.

19          Q.       If you turn the page -- it  
20       might be two pages, let's take a look at  
21       the slides.

22                    Do you know if -- did you  
23       prepare these slides? Do you know who  
24       did it?

1           A.       If I didn't prepare all of  
2       them, I had input to it.

3           Q.       You had, I'm sorry?  You --

4           A.       I would have had input to  
5       it.

6           Q.       Okay.

7           A.       I -- I don't see a signature  
8       who -- who actually prepared the slides.

9           Q.       Okay.  Let's take a look at  
10       the first slide after the title page that  
11       says Background.

12                   Do you see that?

13           A.       Yes.

14           Q.       Page 2.  It says, "There was  
15       an abuse liability expert meeting that  
16       was convened in November of 2003."

17                   Were you present at that  
18       meeting?

19           A.       I was.

20           Q.       Do you recall who the  
21       experts were that attended that meeting?

22           A.       Oh, it was a fair size  
23       group.  I'd have to go back to the  
24       listing.  It would include Nat Katz.

1 Dr. Coleman. I believe Dr. Steve Passik  
2 was there. Again, I couldn't give you a  
3 full listing.

4 Q. Are they -- Dr. Passik is a  
5 key opinion leader?

6 A. Dr. Passik is a psychologist  
7 who is considered an expert in -- in pain  
8 issues.

9 Q. Were the experts that were  
10 invited to the abuse liability panel  
11 meeting all key opinion leaders for  
12 Janssen?

13 A. They were all experts in  
14 their area of -- of concern. So we had  
15 DEA representatives, representatives who  
16 understood regulatory issues, so I -- I  
17 would refer to them as -- as subject  
18 experts.

19 Q. Well, let me ask it a little  
20 differently. Were these experts who had  
21 all been paid by Janssen either in the  
22 past or at the time of this meeting as  
23 either key opinion leaders or subject  
24 experts?

1           A.       Yes.  They -- we would have  
2       had contracts with them to pay for their  
3       consulting services.

4           Q.       And they would have had  
5       those types -- everyone that you named  
6       that was in this, had all had consulting  
7       agreements in the past prior to November  
8       of 2003?

9           A.       I can't say for certain  
10      whether one or more of the individuals,  
11      this might have been the very first time  
12      we contracted with him or her.  I just  
13      don't recall.

14          Q.       Okay.

15          A.       For certain, some of them  
16      had been experts to Janssen previously.

17          Q.       Right.  Some of the names we  
18      recognize from -- correct.

19          A.       Right.

20          Q.       And then if you take a look,  
21      you had -- you had a goal.  And we'll  
22      take a look at some of those studies that  
23      are in the slides that are after this  
24      first slide.

1                   And then outcome, you say,  
2           or someone in the slide says,  
3           "Unanimously agreed that the proposed set  
4           of abuse liability studies under one  
5           year" -- does that mean they would be  
6           completed in under a year?

7                   A.       Yes.

8                   Q.       -- "would by themselves be  
9           convincing evidence of differences in  
10          abuse liability."

11                   Does that mean that the  
12          panel unanimously agreed that the studies  
13          would be convincing?

14                   A.       I believe so.

15                   Q.       But the studies had not yet  
16          been conducted, correct?

17                   A.       That's correct.

18                   Q.       Then the next slide it says,  
19          "At an internal J&J meeting on  
20          January 11th, it was agreed that  
21          differentiating Duragesic from other  
22          transdermal fentanyl systems would  
23          require demonstrations of reduced abuse  
24          liability and improved safety profile

1 to" -- "profile compared to the matrix."

2 Who was present, if you  
3 recall, at the internal J&J meeting?

4 A. I don't recall who was  
5 present. My best assumption would be  
6 that we had representatives of legal,  
7 regulatory, perhaps senior management,  
8 because these had to be funded. The R&D  
9 group, the research and development  
10 group, as well as elements of medical  
11 affairs that might include outcomes  
12 research in the biostatistics group.

13 But I don't know -- I don't  
14 have a recollection exactly who was at  
15 the meeting.

16 Q. Okay. Do you know if anyone  
17 from Europe was present at the meeting?

18 A. More likely than not,  
19 representatives of the R&D group were  
20 present and they represented the global  
21 development of -- of the pain products.  
22 So they would have represented the  
23 fentanyl outside the United States, and  
24 perhaps, again I don't have the listing,

1 represented the -- the group PGSM that we  
2 spoke about, may have been there.

3 Q. What's the difference  
4 between reducing abuse liability and  
5 improving the safety profile?

6 A. So primarily reducing abuse  
7 liability refers to the attractiveness of  
8 one formulation, the reservoir, versus  
9 the matrix. And this would be primarily  
10 to a nonpatient population, if a group  
11 was looking to divert the drug, whereas  
12 the safety profile would refer to both  
13 patients and nonpatients. So for  
14 example, from a safety profile  
15 standpoint, when we spoke about  
16 differences -- potential differences in  
17 delivery of fentanyl if there was a heat  
18 source applied, that might refer to a  
19 patient who accidentally or intentionally  
20 is exposed to a heat source. And -- so  
21 that's what we refer to in the safety  
22 profile.

23 Q. Do you know if any of the  
24 safety profile studies had been conducted

1 in Europe to determine if there were  
2 issues with heat and abrasion with the  
3 matrix patch that was sold by Janssen in  
4 Europe?

5 A. I don't.

6 Q. And would that have been a  
7 place that you would have -- if those  
8 studies did exist, is that a place you  
9 would have looked to make a determination  
10 about the differences between the  
11 reservoir patch and the matrix patch in  
12 the U.S.?

13 A. Potential differences.  
14 There may have been data that were  
15 developed that looked at some of these  
16 issues. But in a laboratory setting, I  
17 don't recall exactly.

18 Q. If you take a look at the  
19 next page, these are the studies that are  
20 being proposed by medical affairs; is  
21 that fair to say?

22 A. Yes.

23 Q. And it would differentiate  
24 Duragesic, which, by saying Duragesic

1       that means the reservoir patch, correct?

2               A.       Correct.

3               Q.       From the matrix and other --  
4       what does MRO stand for?

5               A.       I don't recall.

6               Q.       Do you think it means  
7       something like similar to a matrix patch?

8               A.       In the context of the title,  
9       it would be other formulations of a patch  
10      that delivered fentanyl over an  
11      extended-release period.

12              Q.       That was not a reservoir  
13      patch?

14              A.       It's probably modified  
15      release opioids.

16              Q.       Okay. But in a matrix --  
17      with the matrix technology?

18              A.       No. Because if it's  
19      modified release opioids, then we're also  
20      comparing fentanyl here to other -- not  
21      necessarily fentanyl, other opioids that  
22      are delivered in an extended-release  
23      mechanism.

24              Q.       Like an OxyContin?

1 A. Like OxyContin --

2 Q. Like a continued --

3 A. -- where there's extended  
4 release of oxycodone.

5 Q. And so here, you've spoken  
6 to me about this before. You have the  
7 abuse liability studies that would be  
8 done. And they would determine  
9 attractiveness to an abuser. Is that  
10 what that means?

11 A. Potential attractiveness to  
12 someone who might look to divert the  
13 product or to someone who is seeking to  
14 abuse the product.

15 Q. Extractability, does that  
16 mean how easy or difficult it is to get  
17 the fentanyl out of the -- either the  
18 reservoir or the matrix?

19 A. Yes.

20 Q. And human abuse liability,  
21 what does that mean?

22 A. Similar to attractiveness,  
23 it would be whether the product is more  
24 easily abused than the reservoir patch.

1 Some of the same components about abuse  
2 liability would also -- may also make it  
3 more attractive.

4 Q. Okay.

5 A. I think the concept of  
6 attractiveness doesn't necessarily  
7 include just use of the product. It  
8 would also be how attractive it is to  
9 divert the product, but not necessarily  
10 use it yourself.

11 Q. Would that have anything to  
12 do with the supply of the product, how  
13 available it is?

14 A. Well, it would be how easy  
15 it is to gain access to the fentanyl in a  
16 product, regardless of how you access the  
17 original fentanyl.

18 Q. Okay. So you're talking  
19 about how to get the fentanyl out as  
20 opposed to how accessible a patch might  
21 be?

22 A. Or how easily it is to  
23 transport it too.

24 Q. What does that mean?

1           A.       So let's -- one of the  
2       hypotheses going in, because we knew this  
3       from the report we had from Pinney in  
4       2001, was that in contradistinction to  
5       the reservoir patch where if it was cut,  
6       you'd have leakage of the entire contents  
7       of the patch. A matrix patch could be  
8       cut and give more consistent sizes of the  
9       matrix patch, and, therefore, might be  
10      more easily diverted or sold.

11          Q.       And that's -- you call those  
12      party dots when they put up the matrix  
13      patch?

14          A.       That was one concern that we  
15      had in the context of other drugs of  
16      abuse. We knew at the time that  
17      fentanyl, reservoir patch, was not  
18      attractive in that respect. But we had  
19      concerns that if you could get to a form  
20      that delivered a clear dose, that that  
21      might become more attractive than the  
22      reservoir patch.

23          Q.       And I think I've read in  
24      some of the materials that the Duragesic

1     reservoir patch for an abuser would  
2     really only be able to be sold once  
3     because it would just be the total  
4     release of the fentanyl?

5             A.     It was not an attractive  
6     formulation of fentanyl for a variety of  
7     reasons, which included that it was  
8     difficult to get to a controlled dose of  
9     fentanyl.

10            Q.     Versus the matrix patch  
11     which could be cut into smaller pieces  
12     and each one of those pieces could be  
13     sold and each one of those pieces could  
14     deliver fentanyl?

15            A.     That was the concern.

16            Q.     And then if we look in each  
17     one of the studies on this slide -- is  
18     the first one, abuse liability. And this  
19     is ease of extractability of fentanyl  
20     from transdermal fentanyl systems. So  
21     that's both the reservoir and the matrix,  
22     correct?

23            A.     It was a comparison between  
24     the two.

1           Q.     And objectives are listed.  
2     And then there's the optimal outcome, is  
3     that, "Less fentanyl recovered from the  
4     Duragesic" -- which is the reservoir  
5     patch -- "and it's easier to extract from  
6     the unprotected matrix."

7                     That's what you -- that  
8     would be the best finding for the study,  
9     correct?

10           A.     And we already had some data  
11     to suggest that that would differentiate  
12     the two.

13           Q.     Okay. So it would be --  
14     that would be the optimal, as you say  
15     here, outcome of this study, if you were  
16     attempting to differentiate the reservoir  
17     as a safer -- and I understand safer  
18     means both for the patient and for the  
19     nonpatient -- than the matrix?

20           A.     In a broad sense, yes. When  
21     I'm speaking about safety, I'm talking  
22     not just about the adverse event profile  
23     but the potential for abuse, misuse and  
24     diversion.

1           Q.       Correct. And then you list  
2       your strategic partners. Tell me who  
3       ALZA is.

4           A.       ALZA is --

5           Q.       ALZA.

6           A.       -- the manufacturer of  
7       Duragesic. They were the originators of  
8       the Duragesic patch.

9           Q.       And are they a part of  
10       Janssen or how are they related?

11          A.       Janssen bought ALZA. So it  
12       became a part of Janssen, Johnson &  
13       Johnson. And subsequently it was  
14       subsumed entirely under Janssen.

15          Q.       Where were they physically  
16       located?

17          A.       In California. I believe  
18       it's Mountain View, California.

19          Q.       And who is Bob Bianchi?

20          A.       Bob Bianchi worked with  
21       Inflexxion. He was one of the principals  
22       at Inflexxion and an expert in issues of  
23       abuse liability.

24          Q.       And status, the contract was

1 under negotiation. Who would there need  
2 to be a contract with? Would Inflexxion  
3 be one?

4 A. Yes. Inflexxion was one of  
5 the groups that would develop a study of  
6 attractiveness.

7 Q. And would there need to be a  
8 contract with ALZA?

9 A. Well, with Janssen. Because  
10 we were marketing the product.

11 ALZA produced the product.  
12 Janssen marketed the product.

13 Q. If you -- the budget on this  
14 one is to be determined. If you turn the  
15 page, there's an ease of extractability  
16 study. And the budget was determined to  
17 be \$220,000, correct?

18 Do you see --

19 A. I'm sorry. I see a budget  
20 that says TBD.

21 Q. Go to the next page.

22 A. I'm sorry.

23 Q. Yeah, go to the next page.

24 And then here we have another study on

1 abuse liability.

2 A. Ease of extractability.

3 Q. And -- yeah. And the  
4 strategic partner is Inflexxion.

5 Do you see that?

6 A. Yes.

7 Q. And you have a timeline. It  
8 would take about seven months to do this  
9 study. And the budget that was  
10 determined -- was determined at this time  
11 to be \$220,000, correct?

12 A. Yes.

13 Q. And when you say budget  
14 \$220,000, was that to be paid to  
15 Inflexxion?

16 A. That's my assumption.

17 Q. Were you -- were you also  
18 evaluating what it would cost internally  
19 in medical affairs to -- how does the  
20 budget work?

21 A. Oh no, the -- we wouldn't  
22 budget internal time. This would be what  
23 we would be paying the contract  
24 organization that would be conducting

1       these studies.

2               Q.       Okay. So that would be  
3       money sent out of Janssen to someone  
4       else?

5               A.       Yes.

6               Q.       Go to Page 9, please, which  
7       is abuse liability, again a proposed  
8       study. This is the impact on euphoria  
9       produced by matrix fentanyl via  
10      buccal/sublingual ingestion.

11              Have you found that one? Do  
12      you see that?

13              A.       Yes.

14              Q.       So that is impact of  
15      euphoria if you put it between your gum  
16      and your cheek?

17              A.       Yes.

18              Q.       And who is -- I see the  
19      strategic partner is Dr. Jasinski. Who  
20      is he?

21              A.       A subject expert, not a  
22      Janssen employee.

23              Q.       Okay. Do you know him?

24              A.       I came to know him during

1 the course of the discussions over these  
2 studies.

3 Q. Was this study ever  
4 conducted?

5 A. I don't believe so.

6 Q. Do you know why?

7 A. I can't say for certain.  
8 But I believe it wasn't conducted because  
9 it didn't add to the other data that we  
10 were going to be developing to  
11 differentiate the reservoir from the  
12 matrix.

13 Q. Was the -- was the concept  
14 behind this study that somehow the  
15 reservoir patch, if it was abused and put  
16 between the gum and the cheek, would not  
17 produce as much of a high as if you did  
18 the same thing with the matrix patch?

19 A. That's my assumption because  
20 you would have evaporation of the  
21 alcohol, and the absorption may be  
22 different than the matrix. That's my  
23 best recollection, that in fact we would  
24 show a difference between the two

1 formulations.

2 Q. And you have an optimal  
3 outcome that Duragesic, which is the  
4 reservoir, has a less euphoric effect.  
5 Had you -- did you, like the others, have  
6 some data on that?

7 A. If the concentration of  
8 fentanyl was lower, it should have a less  
9 euphoric effect.

10 Q. And would the concentration  
11 of fentanyl be lower in the reservoir  
12 than in the matrix patch?

13 A. Well, I would say that the  
14 concentration that crosses -- crossed the  
15 buccal mucosa might be lower. The amount  
16 of fentanyl might be the same, but  
17 because of the -- you wouldn't have the  
18 same sticking ability and you don't have  
19 the same formulation that is driving the  
20 fentanyl. So there might be a difference  
21 in -- in the amount of fentanyl that's  
22 transferred.

23 Q. Does the matrix patch  
24 deliver more fentanyl than a reservoir

1 patch?

2 A. If you go back to the  
3 pharmacokinetic studies that showed  
4 bioequivalence, in a healthy volunteer  
5 population, the rate of delivery of  
6 fentanyl is similar between the two  
7 formulations.

8 Q. But if you are putting it  
9 between your gum and your teeth -- or gum  
10 and your cheek, something changes about  
11 the release of the -- something changes  
12 about the amount of fentanyl that's  
13 released?

14 A. That may be the case. This  
15 is what we were considering exploring.

16 Q. What did you already know  
17 about that though?

18 A. Well, we knew there were  
19 oral formulations of fentanyl; Actiq was  
20 one, and so that -- that fentanyl could  
21 be delivered via sublingual or buccal  
22 mechanism fairly quickly. So we  
23 certainly had data for other  
24 formulations.

1           Q.       What -- what I'm talking  
2       about is what did you have that you knew  
3       about the difference in the  
4       concentrations that would be released  
5       between the reservoir and the matrix --

6           A.       I don't know --

7           Q.       -- regardless of where it  
8       was located?

9           A.       No. I don't recall the data  
10       that we had that might have indicated  
11       that there would be a difference between  
12       the two.

13          Q.       Okay. But you did have --  
14       you must have had some data because that  
15       would be the only way that you would be  
16       able to address --

17          A.       Or at least some  
18       hypothetical data that -- towards which  
19       we considered doing this study.

20          Q.       And that hypothetical  
21       data -- what is hypothetical data?

22          A.       It may be data that -- so --  
23       so if we are looking for actual subject  
24       data, the hypothetical data may be data

1     that comes from a laboratory setting, not  
2     in a -- in a human. But data under a  
3     controlled condition -- I'm thinking this  
4     through -- where it may be exposed to  
5     saliva and not in a patient and through a  
6     membrane where you are measuring what  
7     crosses the membrane. That's what I mean  
8     by hypothetical data.

9             Q.     Did -- did Janssen have data  
10    that showed that there were different  
11    amounts of fentanyl that would be  
12    released from a reservoir patch to  
13    between -- reservoir patch and a matrix  
14    patch?

15            A.     Again, if we are talking  
16    about a -- a normal volunteer population.

17            Q.     I understand that. The  
18    normal volunteer population, it's your  
19    understanding it's bioequivalent?

20            A.     Correct.

21            Q.     My question is different.  
22    I'm not talking about a normal. I'm  
23    talking about a patient population or  
24    maybe a lab test. Is there -- does

1 Janssen have any data that would suggest  
2 that there is a greater release of  
3 fentanyl from a reservoir versus a matrix  
4 patch or a matrix versus a reservoir?

5 A. Without having tested it in  
6 a normal volunteer population, we  
7 probably did have laboratory studies  
8 that, for example, might have shown --  
9 again I don't recall -- might have shown  
10 that there was a differential rate of  
11 delivery in a system where heat was  
12 applied.

13 Q. And that would mean that  
14 more fentanyl would be released from a  
15 matrix patch than a reservoir patch?

16 A. Where you are adding heat to  
17 the delivery system.

18 Q. Did Janssen have any data,  
19 not with respect to applying heat or  
20 other types of misuse, that measured the  
21 rate of release of fentanyl from a  
22 reservoir patch versus a matrix patch,  
23 not in a normal volunteer population?

24 A. We -- we had data certainly

1 for the reservoir patch, which is why we  
2 have the warnings, that with heat, you  
3 would have greater delivery of fentanyl.  
4 That's part of the reason we have  
5 warnings for heat delivery.

6 I don't know whether or what  
7 data were developed before the matrix  
8 came to market along the same lines. But  
9 we knew that even with the reservoir,  
10 applying heat would lead to a greater  
11 release of fentanyl across the skin than  
12 without heat.

13 Q. Do you know if there was any  
14 data in Europe with respect to the amount  
15 of fentanyl released from the Janssen  
16 matrix patch?

17 A. Under conditions of --

18 Q. Any -- do you know of any  
19 data at all about the amount of fentanyl  
20 that would be released from the matrix  
21 patch that was -- studies conducted --  
22 conducted in Europe?

23 A. Yes. The pharmaco  
24 equivalent studies, the bioequivalent

1 studies showed that the same amount of  
2 fentanyl would be released with the  
3 matrix patch and -- and a reservoir  
4 patch.

5 If your question is did we  
6 do studies under other conditions, I  
7 don't recall what was done for the matrix  
8 patch relative to the reservoir patch.

9 Q. Do you consider buccal  
10 ingestion to be applying heat?

11 A. It's certainly warmer in the  
12 mouth, but you have other conditions  
13 present as well. I mean it's certainly  
14 misuse of the product.

15 Q. So is your answer no or  
16 you're not certain?

17 A. Well, it's not only that you  
18 have a warmer environment, there are  
19 other factors that are playing into the  
20 potential transfer of fentanyl.

21 Q. Do you have an understanding  
22 based on any data that you have seen why  
23 the Duragesic reservoir would have less  
24 of a euphoric effect?

1           A.       The euphoric effect would be  
2       related to the concentration of fentanyl  
3       in the blood. So any difference in the  
4       euphoric effect would be related to how  
5       much drug is transferred over what period  
6       of time. So even if you have the same  
7       amount, if it's released more rapidly,  
8       that may lead to a greater euphoric  
9       effect.

10           Q.       And the -- the hypothesis  
11       here in this study was that the matrix  
12       would release it faster than the  
13       reservoir patch?

14           A.       That potentially it would.  
15       Again, a lot of the studies overlapped.  
16       So, in fact, that's what we found with  
17       other solvents, that -- in other  
18       solvents, fentanyl in a matrix patch was  
19       released more rapidly and to a greater  
20       degree than it was with the reservoir  
21       patch.

22           Q.       And that would -- that would  
23       create more euphoria?

24           A.       Because it's being released

1 at a more rapid rate, yes.

2 Q. If you turn the page.

3 The -- this is again an abuse liability  
4 study. And the optimal outcome is that  
5 Duragesic has a more aversive effect.

6 This is also to be conducted by  
7 Dr. Jasinski.

8 Aversive effect is -- is an  
9 avoidance effect, is that what it is?

10 A. Yes.

11 Q. And what was -- do you know  
12 if the study was ever conducted?

13 A. It was not.

14 Q. And it was aversive  
15 properties of transdermal fentanyl  
16 systems, so that would be both the  
17 reservoir and the matrix, up at the top,  
18 right -- right underneath the title?

19 A. Okay, yeah.

20 Q. It would be both the  
21 reservoir and the matrix?

22 A. And I'm seeing, again at the  
23 top, so this would be in a subject  
24 population of dependent opiate abusers.

1                   Q.       Correct. That would be  
2       what -- what Dr. Jasinski -- the proposed  
3       study that Dr. Jasinski would perform was  
4       whether there were aversive properties  
5       for both the reservoir as well as the  
6       matrix patch in dependent opiate abusers,  
7       correct?

8                   A.       Whether there were  
9       differences in -- in the aversive effect.

10                  Q.       Okay. And the -- and the  
11       optimal outcome would be that the  
12       Duragesic had more aversive effect. They  
13       were more likely to avoid --

14                  A.       Avoid the Duragesic  
15       reservoir formulation than a matrix  
16       formulation. I guess to flip the same,  
17       that they would prefer the matrix  
18       formulation.

19                  Q.       And do you have -- do you  
20       recall why a dependent opiate abuser  
21       would prefer the matrix?

22                  A.       It was hypothetical, because  
23       the matrix is not on the market. But  
24       again it would relate -- so these are

1 dependent opiate users. They need the  
2 active -- the -- so let's go back to  
3 the -- to the mechanism of action.

4 It is the opiates bind to  
5 the mu opioid receptor. That's what  
6 causes pain relief but potentially leads  
7 to dependence. So these are individuals  
8 who are dependent. That is to say, when  
9 they lack the opiates that occupy the new  
10 receptor, they begin to exhibit symptoms  
11 of withdrawal.

12 So in that population, if  
13 they are using the product that is  
14 releasing fentanyl at a lower rate over  
15 time than another product, in this case  
16 the reservoir versus the matrix, because  
17 they are dependent upon an activation of  
18 the mu opioid agonist, it would be more  
19 aversive to them than a product that  
20 delivered an opioid more rapidly.

21 Q. And so your -- your working  
22 hypothesis was that the reservoir patch  
23 had a lower rate of release of fentanyl  
24 than the matrix?

1           A.       And that would in turn  
2     inform the abuse -- the aversive effect  
3     of the product.

4           Q.       And what -- what data did  
5     you have that showed that there would be  
6     a lower rate of release of fentanyl in  
7     the reservoir patch versus the matrix  
8     patch?

9           A.       Laboratory data that showed  
10    differences in solvents.

11          Q.       And that was laboratory data  
12    at Janssen?

13          A.       It may have been Janssen.  
14    It may have been outside groups that  
15    developed the data and provided those to  
16    Janssen.

17          Q.       And there was something  
18    about the solvents in the reservoir patch  
19    versus the matrix patch that resulted in  
20    less fentanyl being released or being  
21    more slowly released from the reservoir  
22    patch than the matrix?

23          A.       Well, not solvents -- no,  
24    not solvents in the product itself.

1 Solvents that might be used to get access  
2 to the fentanyl. But even within the  
3 product itself, we spoke previously about  
4 the fact that Duragesic had a  
5 rate-limiting membrane, and the  
6 hypothetical matrix patch didn't.

7 So that also might  
8 contribute to a more rapid release of  
9 fentanyl across the buccal mucosa, or  
10 across any membrane, than the Duragesic  
11 reservoir patch.

12 Q. Because the Duragesic  
13 reservoir patch has that thin protective  
14 membrane, correct?

15 A. Rate-limiting membrane.

16 Q. And rate-limiting means that  
17 it was limiting the rate of the release  
18 of the fentanyl?

19 A. Yes.

20 Q. And I just wanted to ask,  
21 one thing that you had said, matrix was  
22 not -- a matrix was not on the market --

23 A. In the United States.

24 Q. -- in the U.S. I just

1       wanted to clarify. It was in the market  
2       in Europe --

3               A.       In Europe.

4               Q.       -- and it would be in the  
5       market in the U.S. in just a few more  
6       years --

7               A.       Yes.

8               Q.       -- after this, correct?

9               A.       Yes. Well, it would be on  
10      the market in a few more months if you're  
11      talking about the generic.

12              Q.       Right. By the other  
13      company.

14              A.       Yes.

15              Q.       Not by -- not by Janssen?

16              A.       Not by Janssen.

17              Q.       Correct.

18              A.       But it came to the market in  
19      January of 2005.

20              Q.       Did Janssen have data  
21      concerning the protective  
22      rate-controlling membrane of the  
23      reservoir patch compared to a patch that  
24      did not have that rate-controlling

1 membrane?

2 A. Only for the reservoir  
3 patch. So we -- I believe that there  
4 were data that compared a reservoir patch  
5 with a rate-limiting membrane, versus a  
6 reservoir patch without a rate-limiting  
7 membrane, but not to a matrix patch  
8 without a rate-limiting membrane.

9 Q. Okay. That latter study was  
10 never done, as far as you know?

11 A. I don't know.

12 Q. Okay. The -- this study  
13 talks about aversive properties of  
14 transdermal fentanyl systems in dependent  
15 opiate abusers. Would you agree with me  
16 that there are also dependent patients  
17 that take -- that use a -- either a  
18 matrix or a reservoir patch?

19 A. Yes. By definition,  
20 dependent means that if you -- if you  
21 withdraw the opiate, stop the delivery of  
22 the opiate, they would exhibit signs of  
23 withdrawal.

24 Q. And that's your definition

1 of dependent, that withdrawal would occur  
2 when the opioid is removed?

3 A. If they no longer receive  
4 the opiate.

5 Q. Turn the page. The next one  
6 are the schema for the safety studies.  
7 And then turn the page again. First  
8 safety study is, "Safety After Chewing an  
9 Unprotected Fentanyl Matrix Versus the  
10 Duragesic Reservoir Matrix," correct?

11 A. Yes.

12 Q. Was this study -- now, this  
13 is another Don Jasinski. Who is Tom  
14 Kosten?

15 A. I'm sure he was a subject  
16 expert. I don't recall exactly what his  
17 affiliation or title was.

18 Q. The optimal outcome here  
19 would be that the Duragesic reservoir  
20 patch, if it was chewed, would have less  
21 of a detrimental effect than if someone  
22 chewed the matrix patch, correct?

23 A. Yes.

24 Q. Was this study ever done?

1 A. No.

2 Q. Do you know why?

3 A. Well, again, in the total  
4 potential studies that were proposed and  
5 evaluated within the context of the  
6 budgets and the timelines, we selected a  
7 subset of studies that were most  
8 relevant. In this instance, just looking  
9 at it today, it probably overlapped in  
10 some instances in data that we would be  
11 generating from some of the other  
12 studies.

13 Q. Do you know if any -- if  
14 there had been any data development prior  
15 to this with respect to chewing either a  
16 reservoir matrix or a -- or the  
17 unprotected matrix -- I'm sorry, a  
18 reservoir patch versus the matrix patch?

19 A. I don't know.

20 Q. Do you know if any studies  
21 had been done in Europe?

22 A. I don't know.

23 Q. The next safety study was  
24 "The Effect of Heat on Fentanyl Release

1 in Duragesic and Fentanyl Matrix." Do  
2 you know if this study was done?

3 A. Yes.

4 Q. It was done?

5 A. It was done.

6 Q. And the optimal outcome was  
7 that Duragesic has less variability. Is  
8 that what was found in the study when it  
9 was ultimately conducted?

10 A. I believe in fact we did  
11 show that there was less fentanyl  
12 transfer using a reservoir patch than a  
13 matrix patch.

14 Q. Do you know what kind of  
15 heat was used?

16 A. I don't recall. It was  
17 probably a heating pad which could be set  
18 specifically to certain temperatures.  
19 But again, I don't want to -- I don't  
20 recall exactly.

21 Q. Okay. Then I see another  
22 safety study. This is the one with  
23 respect to abraded skin. Was that done?

24 A. Not in a human volunteer.

1 This was done, I believe this was done in  
2 rats or mice.

3 Q. Okay. That was also ALZA?

4 A. It was ALZA.

5 Q. And the next slide, this  
6 just tells you when the studies would be  
7 -- sort of a timeline for the proposed  
8 studies?

9 A. Yes.

10 Q. Okay. You can put that one  
11 away.

12 (Document marked for  
13 identification as Exhibit  
14 Janssen-Moskovitz-22.)

15 BY MS. CONROY:

16 Q. I'll hand you Exhibit 22.

17 MS. CONROY: Sorry, folks,  
18 you'll have to use the...

19 BY MS. CONROY:

20 Q. Doctor, this is -- it's hard  
21 to tell. This looks it might have -- I  
22 don't know whether this was slides or a  
23 booklet. It is JAN-MS-00725016. And  
24 it's a technology comparison, reservoir

1       versus the matrix patch system. And it's  
2       sales training, dated February 25th,  
3       2004.

4                       Does this look familiar to  
5       you?

6                       A.       I'm certainly aware of the  
7       information that's here. I can't say  
8       that I've seen this slide deck or this  
9       exact presentation of the data. I'm  
10      certainly aware of the information here.

11                      Q.       And are you aware that the  
12      sales force was trained with respect to  
13      the technological differences between the  
14      reservoir and the matrix patch?

15                      A.       Yes.

16                      Q.       And would they have been  
17      trained sometime around the winter in  
18      2004?

19                      A.       Going by the date on the  
20      first page, that would seem to be the  
21      case.

22                      Q.       Did you yourself ever  
23      conduct or speak at any sales training  
24      conferences or seminars about the

1 differences between the reservoir and the  
2 matrix?

3 A. I don't recall that I did.  
4 I spoke to sales representatives on a  
5 number of topics. I can't say  
6 specifically that I would have spoken to  
7 them on the reservoir versus matrix or  
8 that someone else in my group may have  
9 done that, or that someone in the medical  
10 information group might have done that.

11 Q. Is it fair to say that if a  
12 comparison was done and written up like  
13 this, your eyes would have been on this  
14 at some point?

15 A. We would have reviewed the  
16 information.

17 Q. Did you ever do any webinars  
18 or any sort of video presentations for  
19 the sales force on any particular  
20 matters?

21 A. I don't recall that I did  
22 webinars. Certainly I did some training  
23 at sales meetings, particularly around  
24 clinical trial data. Again, I can't tell

1     you the specifics of each and every  
2     presentation that I might have been  
3     involved with.

4                     I don't recall that I had  
5     any webinars as part of the sales  
6     training. That doesn't mean that I  
7     didn't.

8             Q.     What about any videotaping  
9     of some -- a time when you were speaking  
10    about things so that it could be viewed  
11    by others at a later date?

12            A.     I know that there were  
13    instances where I was videotaped, and I  
14    believe some of those videotapes may have  
15    been for sales training purposes.

16            Q.     Have you ever had any media  
17    training?

18            A.     Yes, I have.

19            Q.     And when did you have that?

20            A.     Oh, at various times over  
21    the course of my being with Janssen, both  
22    on the R&D side and on the medical  
23    affairs side.

24            Q.     And it was -- it was a

1 Janssen though, you weren't -- you  
2 didn't -- this wasn't media training, you  
3 know, for like a rep theater or  
4 something, this was Janssen?

5 A. Yes.

6 Q. Was to do with your job?

7 A. Yes.

8 Q. And if this -- this is just  
9 a -- the key points between the reservoir  
10 and the matrix. And if we can just take  
11 a look, the reservoir has a rate  
12 controlling membrane that you have spoken  
13 to me about. And that regulates the flow  
14 of fentanyl into the skin; do you agree  
15 with that?

16 A. Yes.

17 Q. It just explains there the  
18 fentanyl and alcohol is in a gel. That's  
19 what the reservoir is, correct, a gel?

20 A. It's the composition, yes.

21 Q. It says, "Difficult to  
22 extract pure fentanyl from the patch."

23 Do you agree with that?

24 A. Yes.

1 Q. And did you -- and you had  
2 conducted studies to show that?

3 A. Well, so if you cut the  
4 patch, you are going to be getting the  
5 fentanyl in the cellulose gel and  
6 alcohol. Then you would first have to  
7 purify the fentanyl. So, yes, we knew  
8 that -- that that would require more --  
9 additional steps.

10 Q. Right. Because to get the  
11 fentanyl, you have to get rid of the gel?

12 A. And the alcohol -- the  
13 alcohol and the cellulose gel, yes.

14 Q. "Cutting the patch renders  
15 the system inactive." By that you mean,  
16 if you cut the patch, it renders the  
17 system of extended-release pain relief  
18 inactive?

19 A. The ability to deliver a  
20 controlled release of fentanyl over the  
21 72 hours inactive.

22 Q. And, "13 years of proven  
23 safety." The reservoir patch had been on  
24 the market for 13 years at that point?

1           A.       Since 1990.

2           Q.       "The matrix itself has no  
3       rate-controlling membrane." The drug is  
4       delivered directly into the skin,  
5       correct?

6           A.       Yes.

7           Q.       And is that true today with  
8       a matrix patch?

9           A.       I believe that there are  
10       several formulations of matrix patches.  
11       I can't speak to each and every one of  
12       them. I -- there are matrix patches that  
13       don't have a rate-controlling membrane,  
14       but I can't speak to all of them.

15          Q.       Okay. At the time when this  
16       was written, the matrix patch sold by  
17       Janssen in Europe delivered the drug  
18       directly onto the skin -- or into the  
19       skin, correct?

20          A.       I believe so.

21          Q.       There was no  
22       rate-controlling membrane in the matrix  
23       patch, the Janssen matrix patch in  
24       Europe?

1           A.       I believe so.

2           Q.       Okay. And the -- and a few  
3 years later, the Janssen matrix patch  
4 that was sold in the United States did  
5 not have a rate-controlling membrane?

6           A.       I believe that's correct,  
7 that it was very similar to the matrix  
8 patch that had been sold in Europe.

9           Q.       Are you familiar, at least  
10 until the time you left Janssen in 2011,  
11 of any Janssen matrix patch that had a  
12 rate-control membrane?

13          A.       No.

14          Q.       The next point is "Drug in  
15 adhesive formulation." And then the next  
16 point is "Unforeseeable extraction  
17 methods and implications."

18                 I'm -- I'm questioning this  
19 because I thought we -- we -- there are  
20 foreseeable extraction methods, correct?

21          A.       Yes. Put it in vodka.

22          Q.       Right. So this, this just  
23 means that, to the sales force, that  
24 there are many ways that fentanyl can be

1       extracted from a matrix patch?

2               A.       Ways that we might not even  
3       imagine.

4               Q.       Okay. "Cutting the patch  
5       allows the system to remain intact." And  
6       I think you explained to me why that is a  
7       safety concern, because each one of the  
8       pieces can deliver -- can be sold and  
9       deliver fentanyl?

10              A.       Can be sold and deliver a --  
11       a known quantity of fentanyl.

12              Q.       "Currently marketed matrix  
13       systems are untested with controlled" --  
14       "with CII opioids."

15                      What does -- what do you  
16       mean by that?

17              A.       There were other matrix  
18       systems for other drugs on the market but  
19       they were not Schedule CII opioids.

20              Q.       I see. So the -- the matrix  
21       patch that was either -- at this point  
22       now we are in February of 2004, was  
23       either just going on the market in the  
24       U.S. or it was about to go on the market?

1           A.       No. The matrix -- the  
2       matrix patch didn't go on the market  
3       until January of 2005. There were other  
4       drugs, nonopioids, that were available as  
5       sustained-release formulations to deliver  
6       the drug in a matrix patch, but they were  
7       not opioids.

8           Q.       I see. Okay.

9           A.       So I mean, the technology  
10      was well known, but they -- it had not  
11      been used at this time to deliver an  
12      opioid.

13          Q.       I see.

14                   Turn the page. And I think  
15      that explains some questions I had about  
16      this.

17                   The -- this is talking about  
18      the rate-controlled -- the  
19      rate-controlling membrane in the  
20      reservoir versus the no-rate-controlling  
21      membrane in the matrix.

22                   And then you -- this  
23      explains then why it's important. And  
24      then if you go to the last paragraph, it

1       says, "The currently marketed matrix  
2       delivery systems are untested in real  
3       world prescribing situations with  
4       Schedule II opioids."

5                       That's what you were just  
6       telling me, correct? Because it's been  
7       tested with respect to other drugs,  
8       there's no testing as far as you know  
9       with respect to the delivery of a  
10      controlled substance?

11              A.      Of controlled substances,  
12      yes, that's correct.

13              Q.      "This means that physicians  
14      who choose the matrix are knowingly" --  
15      "are unknowingly investigators in an  
16      overdue safety trial."

17                       Do you see that?

18              A.      Yes.

19              Q.      Had there been any safety  
20      trials of the matrix system with respect  
21      to the delivery of opioids in Europe?

22              A.      I -- I don't know.

23              Q.      Well, it would -- looking at  
24      this, it would suggest to me that Janssen

1 was selling the matrix patch in Europe  
2 without any safety trials.

3 MR. LIFLAND: Object to the  
4 form of the question.

5 THE WITNESS: We were aware  
6 of the fact that there could be a  
7 hypothetical greater release of  
8 fentanyl under special conditions  
9 such as heat, but those conditions  
10 were warned against. It was true  
11 for the fentanyl reservoir patch  
12 as well.

13 What that meant in terms of  
14 a population of nonpatients who  
15 might choose to abuse, misuse or  
16 divert the drug was unknown.

17 BY MS. CONROY:

18 Q. But the -- this one isn't  
19 talking about abuse or diversion. This  
20 is just talking about patients, the --  
21 the matrix system was untested with  
22 respect to the release of a controlled  
23 substance to patients, to legitimate  
24 patients --

1 A. Other than --

2 Q. -- at this time in --

3 A. Well, other than the fact  
4 that we knew even with a reservoir that  
5 under conditions that we warn against  
6 such as heat release, you would have a  
7 greater release of fentanyl than without  
8 those conditions.

9 Q. Correct, but this suggests  
10 to me that the reservoir patch had been  
11 tested with respect to whether or not  
12 controlled substances could be safely  
13 administered to a patient.

14 MR. LIFLAND: Object to the  
15 form of the question.

16 THE WITNESS: I'm not  
17 following exactly your question  
18 because by virtue of the fact that  
19 there were pharmaco-equivalence  
20 studies, bioequivalence studies  
21 that showed under conditions of  
22 appropriate use you would deliver  
23 the same amount of fentanyl. By  
24 virtue of those studies, you are

1           showing similar efficacy and  
2           safety.

3       BY MS. CONROY:

4           Q.       So this -- this statement to  
5       the sales force is not correct, it's  
6       false?

7           A.       No, because we're not  
8       talking about a controlled bioequivalent  
9       study. We're saying in real world --  
10      real world prescribing situations where  
11      we don't know how well the patient has  
12      been instructed on the appropriate use of  
13      the product.

14          Q.       It doesn't say that  
15      anywhere, does it?

16          A.       Well, that's what we mean  
17      by --

18                  MR. LIFLAND: Objection to  
19      the form of the question.

20                  THE WITNESS: That's what we  
21      mean by real world prescribing.  
22      So that's in contradistinction to  
23      a controlled pharmacokinetic  
24      bioequivalent study.

1 BY MS. CONROY:

2 Q. This says that it's untested  
3 in -- "the matrix is untested in real  
4 world prescribing situations." What is  
5 your understanding of a real world  
6 prescribing situation?

7 A. What might happen -- and  
8 here we are talking about the United  
9 States. Again, we already had data that  
10 the environment was different in Europe.  
11 So when we say real world, it's in the  
12 context of the environment in which we're  
13 going to be using the product.

14 There were no data on how --  
15 what would happen in the context of  
16 prescribing a matrix formulation versus a  
17 reservoir formulation other than in a  
18 controlled environment where you're --  
19 where you're showing that the two are  
20 bioequivalent.

21 If the patient accidentally  
22 uses it in a manner other than  
23 prescribed, he or she might have  
24 different outcomes than in the controlled

1 system of a laboratory that's looking at  
2 bioequivalence.

3 Q. In healthy human volunteers.

4 A. Well, that's why I say, in  
5 a -- in a real world patient population,  
6 where we don't know whether the physician  
7 has adequately counseled the patient on  
8 the conditions to avoid, whether that  
9 might lead to different outcomes than  
10 using the reservoir patch.

11 Q. Was a -- was a safety trial  
12 ever done with respect to the matrix  
13 patch in a real world situation with  
14 prescribing physicians?

15 A. In a sense, it was because  
16 we used the matrix patch to gain approval  
17 for pediatric -- for the pediatric  
18 indications. So we had data, safety data  
19 for the pediatric population.

20 Q. And that was later in the  
21 2000s?

22 A. That was -- led to the  
23 approval in 2005.

24 Q. So the pediatric studies had

1       been done by 2005?

2               A.       Were underway and filed so  
3       that the approval came in 2005.

4               Q.       And then why were you  
5       telling the sales force that a physician  
6       who chooses the matrix are unknowingly  
7       investigators in an overdue safety trial,  
8       if you had data that showed that the  
9       matrix was safe?

10              A.       In a pediatric population.  
11      But in the broader -- that's a tiny  
12      fraction of the market.

13                      The broader population, we  
14      can control what we inform the physician  
15      in terms of what he or she needs to do to  
16      educate the patient. But we had concerns  
17      that in real world use, especially if the  
18      drug is diverted outside the patient  
19      population, that there may be adverse  
20      outcomes that we couldn't predict based  
21      upon some of the data that we generated.

22              Q.       I understand that, and I  
23      think we see some of that data and the  
24      effectiveness -- in the attractability

1 and the extraction studies.

2 But this particular sales  
3 force educational piece, doesn't talk  
4 about abuse and diversion. If you look  
5 at the paragraph above, it says, "A  
6 rate-controlling membrane ensures the  
7 system delivers fentanyl at a constant  
8 rate throughout through wearing period,  
9 up to 72 hours, regardless of skin type.  
10 Without the membrane" -- which is the  
11 membrane in the reservoir -- "the skin  
12 itself must regulate drug delivery, which  
13 can lead to variations in delivery from  
14 patient to patient."

15 So this is not talking about  
16 abuse or diversion, correct?

17 A. Correct.

18 MR. LIFLAND: Object to the  
19 form of the question. Let me make  
20 my objection before you start your  
21 answer.

22 THE WITNESS: Okay. I  
23 didn't know that you would object.  
24 I'm sorry.

1 MR. LIFLAND: Well, give me  
2 a moment then. I don't always,  
3 but occasionally.

4 THE WITNESS: When we put  
5 this together, our focus is on  
6 patients. In the back of our  
7 mind, we also recognize that there  
8 is potential for these drugs to be  
9 diverted.

10 So yes, our focus is on  
11 patients, and we were concerned  
12 that if patients didn't follow  
13 appropriate use guidelines, that  
14 there was a concern in that -- in  
15 the patient population that there  
16 would be different outcomes than  
17 with a reservoir.

18 BY MS. CONROY:

19 Q. But the sales force doesn't  
20 know what's in your head, right?

21 MR. LIFLAND: Object to the  
22 form of the question.

23 THE WITNESS: Okay. I'll  
24 grant you that the sales force

1           doesn't know what's in my head.

2           But in putting the slides

3           together --

4       BY MS. CONROY:

5           Q.       So the sales force reading

6           this would not understand that what you

7           may have been thinking about was abuse

8           and diversion?

9                   MR. LIFLAND:   Objection.

10       BY MS. CONROY:

11           Q.       This is --

12                   MR. LIFLAND:   Sorry.

13       BY MS. CONROY:

14           Q.       This is talking about normal

15           use by a physician prescribing it to

16           wear it -- for a patient to wear it for

17           72 hours?

18                   MR. LIFLAND:   Object to the

19                   form of the question.

20       BY MS. CONROY:

21           Q.       Correct?

22           A.       I would take a step back

23           anyways. This is not information that we

24           are instructing a sales representative to

1 have a discussion with a physician. This  
2 is for the sales representative to gain  
3 an understanding of the differences  
4 between a potential matrix and the  
5 reservoir patch.

6 It's purely an educational  
7 opportunity so that they recognize  
8 differences between the systems. It's  
9 not meant for a sales purpose.

10 Q. I thought the whole purpose  
11 of doing these studies was to identify  
12 advantages and disadvantages between  
13 products. Isn't that what the sales  
14 force would be communicating to  
15 customers?

16 A. No.

17 MR. LIFLAND: Object to the  
18 form of the question.

19 THE WITNESS: No, it's not.  
20 That formed the basis of the  
21 Citizen's Petition where we asked  
22 the FDA, that based upon the data  
23 that we generated, there be a  
24 consideration of the potential

1 differences in abuse, misuse, and  
2 diversion between a reservoir  
3 patch and a matrix patch.

4 Those considerations should  
5 go into their decision whether to  
6 approve a matrix patch in the  
7 United States.

8 BY MS. CONROY:

9 Q. And you don't think --

10 A. If they never approved the  
11 matrix patch, the sales force would  
12 continue to sell a reservoir patch.

13 Q. But you don't believe the  
14 sales force would be using that  
15 information between the Mylan matrix  
16 patch and the Duragesic reservoir patch?

17 A. The sales force was  
18 instructed on using the package insert  
19 and the approved promotional materials.  
20 If there was no approved promotional  
21 materials that spoke to differences  
22 between a reservoir patch and a matrix  
23 patch, then they wouldn't be using that.

24 Q. Despite training them on the

1 technological comparisons, correct?

2 MR. LIFLAND: Object to the  
3 form of the question.

4 THE WITNESS: We trained  
5 them on what would be coming down  
6 the pike, if you will. We trained  
7 them on other opioids as well,  
8 even though they weren't selling  
9 other opioids. They needed to  
10 have a broad base of knowledge  
11 about competitive products,  
12 including competitive products  
13 that might be coming to the  
14 market.

15 BY MS. CONROY:

16 Q. Were they precluded from  
17 ever stating any of this information to a  
18 physician?

19 A. If it was not part of  
20 approved promotional materials, they  
21 were.

22 Q. Do you know if there are any  
23 promotional materials that ever described  
24 the differences between the reservoir and

1 the matrix system?

2 A. I don't recall.

3 Q. So if those exist, the sales  
4 force would have been allowed to promote  
5 the product by using a comparison between  
6 the reservoir patch and the matrix patch?

7 A. In theory, yes. And that --  
8 if it existed, it might have been limited  
9 to simply a discussion of the basic  
10 characteristics, that one is in an  
11 alcohol and gel-based system and another  
12 product is available in a  
13 drug-in-adhesive formulation.

14 MR. LIFLAND: Just -- you  
15 don't need to speculate about what  
16 may or may not exist in terms of  
17 answering questions.

18 MS. CONROY: Let's take a  
19 five-minute -- I should say ten  
20 minutes. Not sure.

21 THE VIDEOGRAPHER: Okay.  
22 Off the record, right?

23 The time is 10:53 a.m.  
24 We're going off the record.

1 (Short break.)

2 THE VIDEOGRAPHER: We are  
3 back on the record. The time is  
4 11:34 a.m.

5 BY MS. CONROY:

6 Q. Doctor, I'm going to mark as  
7 the next exhibit, 23, a primary care  
8 franchise update. It looks like a slide  
9 deck with your name on it from June 23,  
10 2004.

11 (Document marked for  
12 identification as Exhibit  
13 Janssen-Moskovitz-23.)

14 MS. CONROY: What did I say  
15 it was, 24? 23.

16 MR. LIFLAND: 23.

17 MS. CONROY: 23.

18 MR. LIFLAND: I guess we got  
19 the Bates number in the back.

20 MS. CONROY: I'm going to  
21 read it into the record. It's at  
22 the back of the document. It's  
23 JAN-MS-00492868.

24 BY MS. CONROY:

1           Q.     Doctor, we see here in the  
2     first slide -- this is -- we saw this in  
3     another slide deck as well. You are the  
4     executive director of the primary care  
5     division of medical affairs at this time,  
6     correct?

7           A.     For the pain products, yes.

8           Q.     For the pain products.

9           A.     And actually, at this time  
10    it included gastrointestinal products. I  
11    can see --

12          Q.     Okay.

13          A.     -- Byron DeLemos was  
14    reporting to me.

15          Q.     So you had some -- you had  
16    some GI products and -- oh, I see over  
17    here. Byron DeLemos --

18          A.     DeLemos.

19          Q.     -- was reporting to you.

20                 And then you have Gary  
21    Vorsanger, senior director. And he  
22    was -- he was working on the pain  
23    products, correct?

24          A.     Yes.

1 Q. And you explained to me  
2 yesterday what medical science liaison  
3 did.

4 Did they -- did medical  
5 science liaison work for -- work with  
6 both the GI products and the pain  
7 products at that time?

8 A. There were -- no, we didn't  
9 have medical science liaisons that worked  
10 on the GI product. The GI products were  
11 legacy products and they were not  
12 actively marketed at the time. But if  
13 there were regulatory reporting  
14 requirements, that fell within my group.

15 Q. And if you take a look  
16 through the slides. And we've seen some  
17 of this information before. If you --  
18 the slides are not numbered. There is  
19 one that says, "Play to Win Strategies."

20 Do you know if that was the,  
21 I'll call it the slogan for the year or  
22 the marketing plan slogan for the year?  
23 Does that have any familiarity with you?

24 A. Very vaguely. I don't

1 recall.

2 Q. Okay. One of the  
3 play-to-win strategies was to  
4 differentiate Duragesic from the generic  
5 matrix patch. Do you see that?

6 A. Yes.

7 Q. And the Duragesic is the  
8 reservoir, correct?

9 A. Yes.

10 Q. And the -- the two points  
11 here are that the patches can be cut  
12 which would be an avenue for diversion  
13 and abuse.

14 Increased opportunities for  
15 misuse. That would be heat issues,  
16 things like that?

17 A. Anything that's not per  
18 package insert, directions on use.

19 Q. And then the second point is  
20 that the fentanyl matrix patches do not  
21 have a rate-controlling membrane, which  
22 we looked at earlier, which means that  
23 the -- the drug is directly on the skin,  
24 correct, there's no rate-controlling

1 membrane like there was in the reservoir  
2 patch?

3 A. That's correct.

4 Q. There's a little bit more on  
5 the next page, there's a little bit more  
6 about that rate-controlling membrane.

7 The rate-controlling  
8 membrane is a key feature of the  
9 Duragesic reservoir patch, correct?

10 A. Yes.

11 Q. And it -- and the -- I take  
12 it the lack of the rate-controlling  
13 membrane could have significant  
14 implications for patient safety. And  
15 that's with respect to patients --  
16 patients who are properly or  
17 appropriately using the product, correct?

18 A. Potentially for patients who  
19 would not be using the product  
20 appropriately.

21 Patients who would be using  
22 the product per package insert, i.e., not  
23 applying heat, not cutting it, the matrix  
24 would deliver the same amount of fentanyl

1 over the same period of time. When we  
2 say patient safety, this is potentially  
3 if they were misusing the drug.

4 Q. So is it your testimony you  
5 were only worried, or you were only  
6 concerned about the existence or  
7 nonexistence of a rate-controlling  
8 membrane with patients who were misusing  
9 the product, not -- by that I mean, and  
10 not legitimate patients appropriately  
11 using the product?

12 A. Thank you. Legitimate  
13 patients appropriately using the product,  
14 we expected that the rate of delivery of  
15 fentanyl would be identical, pharmaco  
16 equivalent to the Duragesic patch. So,  
17 yes.

18 Q. Why didn't you say that?

19 A. Say what?

20 Q. Why did --

21 MR. LIFLAND: Object to the  
22 form of the question.

23 BY MS. CONROY:

24 Q. Why would you say

1     significant implications for patient  
2     safety? Why -- why didn't you  
3     describe -- in the above section you talk  
4     about misuse and diversion, but that does  
5     not appear to be the case in this bullet  
6     point.

7                     MR. LIFLAND: Object to the  
8                     form of the question.

9                     THE WITNESS: This is an  
10                    internal document that updates  
11                    people. I don't know what I might  
12                    have said around these bullet  
13                    points. But certainly there were  
14                    concerns that if patients weren't  
15                    following the appropriate use  
16                    guidelines, that they may be  
17                    exposed to more fentanyl and that  
18                    would represent a patient safety  
19                    issue.

20     BY MS. CONROY:

21                    Q.     You can put that document  
22                    away.

23                             It will be a little bit out  
24                    of order, but let me show you Exhibits 25

1 and 26.

2 (Document marked for  
3 identification as Exhibit  
4 Janssen-Moskovitz-25.)

5 (Document marked for  
6 identification as Exhibit  
7 Janssen-Moskovitz-26.)

8 BY MS. CONROY:

9 Q. 26 is a cover letter from  
10 Gayatri Sathyan to Gary Vorsanger, and  
11 you are on the cc list. And it actually  
12 attaches the -- Dr. Allcorn Mudskipper  
13 White Paper.

14 And then Exhibit 27 -- I'm  
15 sorry. 25 is the confidential draft  
16 document, White Paper. And it's the  
17 August 16, 2004, draft.

18 The -- Exhibit 26 is  
19 JAN-MS-021029711, and the White Paper,  
20 Exhibit 25, is JAN-MS-02109712, and it's  
21 an attachment to Exhibit 26.

22 MR. LIFLAND: No, actually  
23 she's going to hand you --

24 MS. CONROY: I'm going to

1 hand you this one so that you have  
2 the stickers. So the title --

3 MR. LIFLAND: Sorry. The  
4 first page is 25, and the next one  
5 is --

6 MS. CONROY: No. The first  
7 page is 26. The attachment is 25.

8 MR. LIFLAND: Okay. Thank  
9 you.

10 BY MS. CONROY:

11 Q. If we take a look at  
12 Exhibit 26 first, the cover letter.

13 I'm sure I've butchered the  
14 name. Gayatri Sathyan, who is that?

15 A. It was an ALZA  
16 representative. I don't recall  
17 exactly -- based upon the totality of  
18 what I'm looking at, probably somebody  
19 who was working in the pharmacokinetic  
20 group or assessment of -- of drug  
21 delivery systems.

22 Q. And we know who  
23 Dr. Vorsanger is?

24 A. Yes.

1           Q.     And Suneel Gupta in -- is  
2     also at ALZA?

3           A.     Yes.

4           Q.     You can tell that from the  
5     address?

6           A.     Yes.

7           Q.     And then I think you told me  
8     Clare Harte is in medical affairs as  
9     well; is that correct?

10          A.     That's correct. She was in  
11     the operations group, and she had some  
12     overall responsibility with the  
13     contracting with the various  
14     organizations that we work with and with  
15     the operational side of getting the data  
16     and collating the data.

17          Q.     If you look below, Clare had  
18     sent some slides around. And then she  
19     asked at least the folks on the e-mail --  
20     it doesn't look like you are on the  
21     e-mail. "Check the accuracy of the  
22     slides and the pharmacokinetic section of  
23     the White Paper of this most recent  
24     draft." And then --

1                   A.       Excuse me.

2                   Q.       Bless you.

3                           And then it looks like the  
4   ALZA individual writes, and includes you  
5   on it, to Dr. Vorsanger and also Clare  
6   Harte that there were some comments on  
7   the White Paper. Number one, "The heat  
8   study that showed no major difference  
9   between the two formulations is basically  
10  being ignored."

11                           And I'm trying to understand  
12  what that means. Did the heat study data  
13  show that there was not a difference with  
14  respect to release between the reservoir  
15  and the matrix patch?

16                   A.       I don't recall. I'd have to  
17  go back to the studies.

18                   Q.       And then do you recall any  
19  issue concerning where to put the patch  
20  with respect to delivery of the drug?

21                   A.       There are guidelines in the  
22  package insert about where to put the  
23  drug and how to rotate the attachment  
24  site.

1           Q.     Have you ever heard about a  
2     difference between putting it on the arm  
3     versus the back versus the chest?

4           A.     There were potentially  
5     differences because of blood flow in the  
6     area that could lead to slight  
7     differences in the absorption of the  
8     fentanyl.

9           Q.     Do you know -- it says here,  
10    "We can speculate such a difference would  
11    not show up for the reservoir, but we  
12    don't have data."

13                   Do you know if any data was  
14    ever collected with respect to whether  
15    there would be a difference with respect  
16    to drug delivery between the arm, the  
17    back, or the chest?

18           A.     I don't recall.

19           Q.     Let's take a look at the  
20    White Paper itself.

21                   MR. LIFLAND:   For the  
22                   record, this is 25?

23                   MS. CONROY:   This is  
24                   Exhibit 25.   That's right.

1 BY MS. CONROY:

2 Q. So the title of this is  
3 "Transdermal Fentanyl Systems," which at  
4 this time would be the reservoir with the  
5 protective rate-controlled membrane and  
6 the matrix that did not have a  
7 rate-controlling membrane, correct?

8 A. It would be the reservoir  
9 and hypothetical matrix systems. There  
10 was nothing marketed at the time.

11 Q. Well, there was a matrix  
12 system marketed in Europe?

13 A. Correct. But the studies  
14 that were done in here, we didn't have  
15 access to the matrix product that would  
16 be marketed in the United States.

17 Q. So what did you --

18 A. We used the product that was  
19 available in Europe.

20 Q. So you used the Janssen  
21 matrix for these studies? So you  
22 compared the Janssen matrix to the  
23 Janssen reservoir?

24 A. Yes.

1                   Q.       And it was your  
2       understanding, at least, that the Janssen  
3       matrix that you used for these studies  
4       was equivalent to what you expected to be  
5       sold as a matrix product in the United  
6       States?

7                   A.       Ultimately there were very  
8       minor differences, because I believe that  
9       the pharmacokinetics studies that showed  
10      bioequivalence, there was an  
11      intermediate -- I'm not certain. I think  
12      there were minor differences in the patch  
13      that we ultimately brought to market, the  
14      matrix patch that we ultimately brought  
15      to market from the matrix patch that was  
16      marketed at this time in Europe. But I  
17      don't know the specifics of it.

18                  Q.       What do you know about that?  
19      Was -- was there an attempt to make the  
20      U.S. Janssen matrix patch somehow  
21      different than the European Janssen  
22      matrix patch?

23                  A.       I don't recall that there  
24      was any attempt to. It may have been

1 related to excipients. But I don't  
2 recall. I have a vague recollection that  
3 we couldn't simply manufacture identical  
4 matrix patch in the United States to what  
5 was being marketed in Europe, and that  
6 there were -- there was a bioequivalency  
7 study that looked at an intermediate  
8 product, and that to the one in the  
9 United States.

10 My recollection of that is  
11 really vague because it was all done  
12 within the formulations group.

13 Q. When you say an intermediate  
14 product, where was -- is that a U.S.  
15 intermediate product?

16 A. Again, I don't know the  
17 steps.

18 Q. Okay. Do you know if there  
19 was ever a bioequivalency test performed  
20 at any time between the Janssen European  
21 matrix and the Janssen U.S. matrix when  
22 they were both on the market?

23 A. Yes. Again I have a vague  
24 recollection that there was a

1 bioequivalency study done between the  
2 marketed matrix product in Europe to a  
3 matrix product to be marketed in the U.S.  
4 and then a subsequent study between the  
5 matrix product to be marketed in the  
6 U.S., which was bioequivalent to the  
7 European matrix. And that product to the  
8 U.S. reservoir. Again, I don't have -- I  
9 don't have enough recollection of that  
10 because most of the work was done in the  
11 formulations group.

12 Q. Is it your understanding  
13 that the European matrix patch was  
14 bioequivalent to the Janssen matrix patch  
15 in the U.S.?

16 A. Yes.

17 Q. The remainder of the title  
18 here is, "Reduced safety and increased  
19 societal risk of matrix patch  
20 formulations."

21 Would that include the  
22 matrix patch formulations in Europe?

23 A. These were hypothetical and  
24 in some cases, you know -- based upon

1 data that we generated over the course of  
2 late 2003, 2004, that led us to believe  
3 that there were different risks  
4 potentially reducing the safety of a  
5 matrix patch relative to the reservoir  
6 patch in the context of the U.S.  
7 environment.

8 Q. Right. The patches were the  
9 same, it was the patients that were  
10 different; is that correct?

11 A. Or how it was used or how it  
12 might be diverted and misused.

13 Q. But the patches are the  
14 same?

15 A. The patches --

16 Q. The matrix patch in Europe  
17 is the same --

18 A. -- as the matrix patch that  
19 we used as a testing mechanism, where  
20 we -- where we used the matrix patch. In  
21 the studies of attractiveness, it was a  
22 description.

23 Q. This front sheet has  
24 Mudskipper Strategies. That's

1 Dr. Allcorn that we spoke about earlier,  
2 correct?

3 A. Who is the principal of  
4 Mudskipper, yes.

5 Q. And you read through this  
6 draft White Paper Exhibit 25, correct?

7 A. Yes.

8 Q. Carefully, correct?

9 A. Yes.

10 Q. If we turn to Page 11, over  
11 into the next page, but it states here,  
12 "We believe" -- "we" is Janssen, correct?

13 A. Janssen, ALZA, yes. And  
14 certainly from -- with respect to  
15 reservoir and our assessment. Let's say  
16 Janssen.

17 Q. Okay.

18 -- "taken together, this  
19 information" -- which the information is  
20 the comparison between the reservoir  
21 patch and the matrix patch, correct?

22 A. Yes. And in another  
23 instance also relative to other  
24 extended-release, other opioids.

1           Q.       -- "demonstrates not only  
2     that Duragesic" -- and that means the  
3     reservoir patch, right?

4           A.       Yes.

5           Q.       -- "and fentanyl matrix  
6     patches are not interchangeable in the  
7     clinical setting but that matrix patches  
8     present an unacceptable risk" --  
9     "additional risk both to patient safety  
10    and public health in the United States."  
11                   Do you see that?

12          A.       Yes.

13          Q.       And do you still agree with  
14    that statement?

15          A.       We subsequently developed  
16    data to show that the concerns we had at  
17    this time didn't materialize. So I would  
18    say that no, I no longer believe that.

19          Q.       Okay. What data did you  
20    prepare or collect?

21          A.       You are talking about  
22    subsequent?

23          Q.       Yes, that made you abandon  
24    this.

1           A.       So as part of our commitment  
2       to the Food and Drug Administration, we  
3       continued to market the reservoir in the  
4       United States, even after there was a  
5       generic matrix fentanyl patch that came  
6       to market.

7                       As part of our commitment,  
8       we had in place a number of surveillance  
9       systems, some of which we spoke about  
10      yesterday, DAWN, the key informant  
11      network, examination of internet  
12      websites, laboratory assessments. And we  
13      monitored that for several years.

14                    At one point the FDA  
15      requested that we shift from our  
16      reservoir patch to a matrix patch. And  
17      we contended at the time that we had the  
18      same concerns that we brought to the  
19      FDA's attention in the Citizen's Petition  
20      that we filed in 2004.

21                    We at that time said to the  
22      FDA, Well, okay, now we have several  
23      years of data available to us from our  
24      surveillance program, which to a great

1 degree was able to differentiate between  
2 the marketed matrix on the -- in the  
3 United States and the reservoir patch,  
4 and when we evaluated those data, we  
5 concluded that the concerns we had about  
6 increased risks of --

7 (Brief interruption.)

8 THE WITNESS: I'm sorry.

9 -- increased risks for  
10 abuse, misuse and diversion had  
11 not materialized, and, therefore,  
12 we felt comfortable in moving  
13 ahead with the FDA's request that  
14 we shift our own Duragesic  
15 reservoir patch to a matrix patch  
16 in the United States.

17 BY MS. CONROY:

18 Q. So you became comfortable  
19 that there was no increased risk of  
20 diversion with respect to the matrix  
21 versus the reservoir, correct?

22 A. We had surveillance data  
23 that did not show an increased risk for  
24 abuse, misuse and diversion with the

1 matrix patch.

2 Q. Correct. And then at one  
3 point only the matrix patch is available  
4 for sale in the United States with, you  
5 know, with controlled substance?

6 A. I -- it was my understanding  
7 that there was another generic patch for  
8 a time that was a reservoir patch, but at  
9 some point they moved from that as well.  
10 We weren't the only reservoir patch on  
11 the market, but I don't recall the timing  
12 for their switch either.

13 Q. But at some point Janssen  
14 switched and only sold the matrix patch,  
15 no longer sold the reservoir patch?

16 A. That's correct.

17 Q. What studies indicated to  
18 you that the matrix patch, after the  
19 reservoir was no longer being sold, was  
20 not attractive to abusers?

21 A. We had surveillance data,  
22 the surveillance mechanisms that we had  
23 put in place in 2005 as part of our risk  
24 management program that looked at DAWN

1 data, that looked at internet monitoring  
2 data, that looked at the NFLIS data  
3 around laboratories, and it did not show  
4 a difference in rates of abuse, misuse  
5 and diversion between the matrix patch  
6 and the reservoir patch.

7 Q. That -- that wasn't actually  
8 my question.

9 My question is what data  
10 showed you that there was not abuse and  
11 diversion with the matrix patch that was  
12 being sold by Janssen in the United  
13 States.

14 MR. LIFLAND: Object to the  
15 form of the question.

16 THE WITNESS: And -- so we  
17 had data that showed there was no  
18 difference in rates of abuse,  
19 misuse and diversion. All of the  
20 surveillance showed a small degree  
21 of abuse, misuse, diversion  
22 adverse events, but we were  
23 concerned about potential  
24 differences between the two and

1           those didn't materialize based  
2           upon our surveillance.

3       BY MS. CONROY:

4           Q.     And -- and I understand  
5           that, and if you take a look at Page 11,  
6           the statement is, "Matrix patches present  
7           an unacceptable additional risk both to  
8           patient safety and public health in the  
9           United States."

10                  What changed about the  
11           matrix patch that made it not an  
12           unacceptable additional risk to patients  
13           in the U.S.?

14           A.     Perhaps nothing. At the  
15           time that we did this report, it was all  
16           based upon hypothetical data. There was  
17           no matrix patch that was available in the  
18           United States.

19                  So all of the studies that  
20           we did through 2003 and 2004 looked at  
21           hypothetical risks associated with the  
22           matrix patch.

23                  The FDA nonetheless approved  
24           a generic matrix patch. They responded

1 to our Citizen's Petition and justified  
2 why they were moving ahead with approving  
3 a matrix formulation of -- of transdermal  
4 fentanyl. And we did not at the time  
5 switch.

6 But because of the  
7 hypothetical concerns that we learned of  
8 during the course of our studies, we  
9 continued to monitor for those  
10 differences. And our -- at this time, we  
11 were concerned that introducing a matrix  
12 formulation would lead to increases in  
13 additional risks to the patient  
14 population or to the public health by  
15 virtue of differences in diversion and  
16 abuse, but they didn't materialize.

17 Q. So what you don't agree with  
18 any longer on Page 11 is the reservoir  
19 and the fentanyl matrix patches may be,  
20 in your estimation, they are  
21 interchangeable?

22 A. That the risks that we -- we  
23 knew that pharmacokinetically they were  
24 equivalent. But we were concerned about

1 other risks associated with misuse, abuse  
2 and diversion. They didn't materialize.  
3 And until we convinced ourselves that the  
4 risks that we were concerned about when  
5 we did the early studies with the  
6 hypothetical matrix in the United States,  
7 it didn't materialize. And therefore, we  
8 felt comfortable moving, per the FDA's  
9 request, in switching from our Duragesic  
10 reservoir patch to a matrix patch.

11 Q. So those risks cease to  
12 exist with the matrix --

13 A. They never -- they never  
14 materialized.

15 Q. So they --

16 A. And I won't say they ceased  
17 to risk. There were risks associated  
18 with the reservoir patch and with the  
19 matrix patch. We were looking at whether  
20 there were significant differences in  
21 those risks. Differences in rates of  
22 those risks. We did not see a difference  
23 in the rates of those risks.

24 Q. But you saw no decrease in

1 the rates with respect to the matrix  
2 patch?

3 A. I believe our conclusion was  
4 that there was -- that once we reviewed  
5 the surveillance data, that we concluded  
6 that there was no additional risk.

7 Q. Was there an issue with the  
8 data with the ability to differentiate  
9 between the reservoir patch and the  
10 matrix patch?

11 A. My understanding is  
12 initially there was and we worked with  
13 the colleagues who did the surveillance  
14 program because we pushed them to the  
15 extent possible to differentiate between  
16 the -- the generic matrix patch and the  
17 branded reservoir patch.

18 Q. And approximately how many  
19 months were both on the market in the  
20 U.S.?

21 A. Before we switched to a  
22 matrix patch?

23 Q. Correct.

24 A. May I go back to see exactly

1       when we brought the matrix patch?

2                       Okay.    So in 2009 we -- we  
3       brought the matrix patch.    Sometime  
4       before that the FDA requested that we  
5       switch from the reservoir patch.    But  
6       certainly between 2005 and 2009 the  
7       matrix patch in a generic formulation was  
8       available in the United States.    So we  
9       would have had data on several years of  
10      surveillance.

11               Q.       And the FDA, as you state,  
12      requested a change from the reservoir  
13      patch to the matrix patch because of two  
14      recalls for leaking fentanyl from the  
15      reservoir patch?

16               A.       Because of manufacturing  
17      issues associated with the Duragesic  
18      reservoir patch, that's correct.

19               Q.       Did your analysis of the  
20      data from 2005 to 2009 show any  
21      differences in the manner of diversion  
22      that you studied in this White Paper, the  
23      attractiveness or the extractability?

24               A.       Well, it wouldn't show

1 differences in extractability. That's a  
2 laboratory control. The differences we  
3 saw in extractability led us to believe  
4 that there might be differences in the  
5 real world availability of the two. But,  
6 in fact, in the surveillance systems we  
7 put in place, we didn't see the  
8 additional risks associated with  
9 differences in -- in availability under  
10 those conditions.

11 Q. Did you still see in that  
12 data support for the attractiveness of  
13 the matrix patch?

14 A. Based upon the surveillance  
15 systems we had in place, we didn't see  
16 that the matrix patch was being abused,  
17 misused, or diverted at a rate  
18 substantially different from the  
19 reservoir patch.

20 Q. I understand that, but did  
21 you see any difference with respect to  
22 the attractability of the matrix patch to  
23 abusers? And I'm -- I'm not talking  
24 about in comparison with the reservoir

1 patch. I'm just talking about whether or  
2 not your hypothesis about why the matrix  
3 patch would be attractive to abusers held  
4 up when you looked at the data.

5 A. Well, we --

6 MR. LIFLAND: Object to the  
7 form of the question.

8 THE WITNESS: We didn't  
9 measure attractiveness.  
10 Attractiveness was a measure in  
11 the studies of whether a drug was  
12 more attractive. If a drug was  
13 more attractive, then  
14 theoretically that drug would be  
15 sought more so than a comparator  
16 drug, whether that be Duragesic  
17 reservoir or another  
18 extended-release opioid.

19 So although we didn't  
20 surveil for attractiveness, we --  
21 our surveillance was able to pick  
22 up measures of abuse, misuse, and  
23 diversion.

24 In those measures, we didn't

1           see a significant difference  
2           between the two formulations. It  
3           doesn't say that the matrix patch  
4           is or is not more attractive.  
5           Within the environment of the  
6           United States, it may -- it may be  
7           that availability of other drugs  
8           that are far more attractive  
9           overrides the concerns between  
10          differences in the reservoir or  
11          matrix patch.

12                       We simply didn't see  
13           differences in rates of abuse,  
14           misuse and diversion. We didn't  
15           measure attractiveness in any  
16           surveillance system.

17 BY MS. CONROY:

18           Q.       Do you know if the street  
19           value of the matrix patch changed at all  
20           from your evaluation? And it's on Page  
21           61 of the White Paper.

22           A.       I don't know.

23           Q.       Then if you -- there's a --  
24           you'll see there are calculations on the

1 value of a cut matrix patch. Do you know  
2 if there were any --

3 A. I'm sorry. I'm afraid --  
4 what page are you on?

5 Q. 61 and 62.

6 A. Okay.

7 Q. 61, you see, at the top --  
8 it talks about the -- 60 -- Page 62, the  
9 economics of diversion of fentanyl matrix  
10 patches?

11 A. Somehow we're not looking --  
12 this is my Page 62.

13 Q. Yeah. Go page 61.

14 A. Okay. Okay. That's under  
15 section 6.2.2.2?

16 Q. Yes. So take --

17 A. Okay.

18 Q. Take -- it says, "Economics  
19 of" --

20 A. Yep.

21 Q. -- "diversion of fentanyl  
22 matrix patches."

23 A. Yes. Okay.

24 Q. Okay. And then it talks

1 about the number of units that could be  
2 cut?

3 A. Yes.

4 Q. Was there anything -- was  
5 there any data that was ever collected  
6 that indicated that that did not continue  
7 to be true about the matrix patch?

8 A. No. We -- all of these data  
9 were hypothetical. We didn't collect  
10 data on the street value of a matrix  
11 patch of fentanyl. We collected data on  
12 actual abuse, misuse and diversion.

13 Q. Was there anything that  
14 indicated there was not still abuse,  
15 misuse and diversion of the matrix patch  
16 in the data that you reviewed?

17 A. No. We continued to see  
18 measures of -- and rates of abuse, misuse  
19 and diversion for both the Duragesic  
20 reservoir patch and the matrix patch, but  
21 we didn't see substantial differences  
22 between the two.

23 Q. If you look on Page 84,  
24 Number 6 here, "Availability of a

1     fentanyl matrix patch is likely to  
2     increase the diversion of patches with  
3     major" -- "with major public health  
4     consequences for expansion of the current  
5     market for illicit fentanyl and the  
6     creation of new markets for illicit  
7     fentanyl use."

8                     Do you see that?

9             A.     Yes.

10            Q.     Any reason to believe that  
11     that -- that statement or statements are  
12     not -- do not continue to be true?

13            A.     Again, just in terms of the  
14     surveillance that we had in place to  
15     monitor for abuse, misuse and diversion,  
16     we did not see differences between the  
17     matrix patch and the reservoir patch.

18                     Fentanyl continues to be a  
19     potent Schedule II opioid that's sought  
20     by drug abusers, and that was true after  
21     the matrix was introduced and at the time  
22     that Duragesic was on the market. But we  
23     didn't see differences when we did our  
24     surveillance program. We continued to

1 see use of illicitly obtained fentanyl,  
2 but couldn't directly attribute that to a  
3 matrix patch or a reservoir patch.

4 Q. Did you -- when you reviewed  
5 the data after 2004 when this was  
6 prepared, did you see that the  
7 availability of a matrix patch increased  
8 diversion activity --

9 A. No, we --

10 Q. Did you see an increase in  
11 diversion?

12 A. The systems we had in place  
13 monitored for abuse, misuse and  
14 diversion. We didn't see differences in  
15 rates of diversion between the matrix  
16 patch and the reservoir patch.

17 Q. That's not my question.

18 A. I understand. So we weren't  
19 monitoring for expansion of the market  
20 for illicit products. We -- the  
21 surveillance mechanisms did pick up that  
22 there was fentanyl that was abused,  
23 misused, and diverted that was illicitly  
24 obtained fentanyl. And we knew that

1     illicitly obtained fentanyl was sought  
2     after.

3                     But where we had  
4     surveillance data specifically for the  
5     matrix and the reservoir, we didn't see  
6     differences between those two. Yes, we  
7     knew that illicitly obtained fentanyl  
8     increased over time.

9                     Q.     So this -- this ended up  
10    being true, Number 6, that the  
11    availability of the matrix patch  
12    increased the diversion of patches if you  
13    saw in your data that there was increased  
14    diversion of illicit fentanyl?

15                    MR. LIFLAND: Object to the  
16                    form of the question.

17                    THE WITNESS: You can't  
18                    correlate -- you can't show cause  
19                    and effect between availability of  
20                    pharmaceutical grade Duragesic,  
21                    whether it's in a matrix patch or  
22                    a reservoir patch, to the use of  
23                    illicitly obtained fentanyl. That  
24                    may relate to lots of other

1           potential contributing factors,  
2           such as availability of heroin on  
3           the market or availability of  
4           other products that are laced with  
5           a very potent formulation of  
6           fentanyl. So we could not  
7           conclude anything between the  
8           availability of pharmaceutical  
9           grade fentanyl as a matrix patch  
10          or a reservoir patch and the use  
11          of illicitly obtained fentanyl.

12       BY MS. CONROY:

13           Q.     If you couldn't determine  
14          whether there was diversion of pharma  
15          grade fentanyl versus illicit fentanyl,  
16          how could you make the determination that  
17          there was not a distinction between the  
18          reservoir matrix -- the reservoir and the  
19          matrix --

20           A.     Because --

21           Q.     -- if you can't  
22          differentiate pharma grade?

23                   MR. LIFLAND: Object to the  
24          form of the question.

1 THE WITNESS: Because in  
2 some of the surveillance programs,  
3 they would report to us if they  
4 discovered that it was Duragesic  
5 or the Mylan early on, and other  
6 generic formulations of  
7 pharmaceutical grade patches.

8 They had the ability to  
9 report to us if there was  
10 diversion of those systems, or if  
11 those systems were in use.

12 So based upon those  
13 surveillance programs where they  
14 were able to differentiate the  
15 product that was being abused,  
16 misused, and diverted, we didn't  
17 see a difference between the two  
18 formulations.

19 BY MS. CONROY:

20 Q. And using those same  
21 programs, were you able to determine  
22 whether or not pharma grade -- the  
23 diversion of pharma grade fentanyl was  
24 increasing over time up until 2009?

1           A.       I'd have to go back to the  
2       reports. It's my understanding that  
3       there were increases over time of abuse,  
4       misuse and diversion for formulations of  
5       Duragesic. And that's what we warned  
6       against. That's why we strengthened our  
7       package insert over time, because of the  
8       concerns with increasing use of strong  
9       opioids and the issues around abuse,  
10      misuse and diversion.

11           Q.       Correct. And so this --  
12      what you talked about in 2004 apparently  
13      was reflected in the data in 2009, that  
14      the availability of a fentanyl matrix  
15      patch is likely to increase the diversion  
16      of patches?

17                   MR. LIFLAND: Object to the  
18                   form of the question.

19      BY MS. CONROY:

20           Q.       You saw that?

21                   MR. LIFLAND: Object to the  
22                   form of the question.

23                   THE WITNESS: I disagree  
24                   that you're showing that by virtue

1 of making a matrix patch  
2 available, that that led to the  
3 increase in expansion of the  
4 market for illicit fentanyl.  
5 There's no cause and effect there.

6 That's as if saying that had  
7 there never been a matrix  
8 formulation brought to market, if  
9 the Duragesic reservoir patch  
10 remained on the market, we would  
11 not see any increase in illicit  
12 fentanyl use. I can't say that  
13 that would have been the case. I  
14 can only say that when a matrix  
15 formulation of Duragesic, when it  
16 was introduced to the market, we  
17 didn't see differences between the  
18 two.

19 BY MS. CONROY:

20 Q. I know. But you did say  
21 this, you did say that there would be a  
22 likely increase in the diversion of  
23 patches once the fentanyl matrix patch  
24 was available.

1 A. That was our --

2 MR. LIFLAND: Object to the  
3 form of the question.

4 THE WITNESS: That was our  
5 hypothetical concern based upon  
6 the attractiveness scale and  
7 the -- and the knowledge we had  
8 that you could cut a matrix patch  
9 more readily than you could a  
10 reservoir patch.

11 BY MS. CONROY:

12 Q. And you did see data in 2009  
13 that there was an increased diversion of  
14 pharma grade fentanyl?

15 A. Yes, but I can't attribute  
16 that to availability of a matrix patch.

17 Q. Because it hasn't been  
18 tested, correct?

19 MR. LIFLAND: Object to the  
20 form of the question.

21 THE WITNESS: Illicitly  
22 obtained fentanyl would be very  
23 difficult to test. We don't know  
24 where the drug is coming from.

1           And in many instances, it's  
2           co-mixed with heroin and other  
3           drugs of abuse. I'm not sure how  
4           you would test that the  
5           availability of pharmaceutical  
6           grade fentanyl would lead to an  
7           increase in illicitly used  
8           fentanyl.

9       BY MS. CONROY:

10           Q.       Apparently Mudskipper  
11       thought they could figure that out.

12                   MR. LIFLAND: Object to the  
13       form of the question.

14                   THE WITNESS: Well,  
15       Mudskipper didn't figure it out.  
16       We were talking about their simply  
17       summarizing the data.

18                   Based upon what we knew of  
19       the matrix formulation and other  
20       studies we did, such as the  
21       attractiveness, there was a  
22       hypothetical risk that individuals  
23       who were interested in abusing,  
24       misusing or diverting opioid

1 medications, including the  
2 Duragesic patch or matrix, would  
3 find the matrix patch to be more  
4 attractive for abuse, misuse and  
5 diversion.

6 If they had access to -- if  
7 they wanted a fentanyl product and  
8 had access to other fentanyl, such  
9 as illicitly obtained fentanyl,  
10 perhaps they would go there.

11 I can't make a direct  
12 correlation between pharmaceutical  
13 grade fentanyl and illicitly  
14 obtained fentanyl.

15 I can only speak to what we  
16 studied here which was whether  
17 there were potential differences  
18 between these two formulations.  
19 We, in our studies, found  
20 potential differences that  
21 informed our conclusion that there  
22 may be risks associated with the  
23 matrix that were going to be  
24 greater than risks associated with

1           the reservoir patch. And we  
2           brought those concerns to the FDA  
3           in our Citizen's Petition.

4       BY MS. CONROY:

5           Q.     To date, are you aware of  
6           any studies sponsored by Janssen that the  
7           matrix patch has not increased the  
8           diversion of patches?

9                     MR. LIFLAND: Object to the  
10           form of the question.

11                    THE WITNESS: No.

12       BY MS. CONROY:

13           Q.     Turn to Page 90. Do you see  
14           where it says, "The parallels between  
15           OxyContin" -- and that's a  
16           controlled-release pill, correct?

17           A.     Controlled-release pill that  
18           delivers Oxycodone.

19           Q.     -- "and the Mylan patch are  
20           clear."

21                     Were -- were there studies  
22           done that compared the Mylan patch to  
23           OxyContin?

24           A.     Not to my knowledge.

1 Q. And Janssen did not have a  
2 Mylan matrix -- matrix patch to test at  
3 this time; is that correct?

4 A. That's correct.

5 Q. Do you know if that testing  
6 was ever done, a comparison between  
7 OxyContin and the Mylan matrix patch at  
8 Janssen?

9 A. For what reason? When we  
10 talk about parallels, we are not talking  
11 about a clinical trial, we're talking  
12 about a hypothetical understanding of  
13 Oxycodone and extended-release Oxycodone,  
14 what was known about OxyContin and what  
15 was known about Duragesic and the data  
16 that we generated through our studies on  
17 a hypothetical patch, that we expected  
18 would be coming to market in the 2005  
19 time frame.

20 Q. Do you know if there were  
21 ever any clinical studies or trials that  
22 compared OxyContin to the Janssen matrix  
23 patch?

24 A. There were not.

1           Q.     Do you know if there were  
2     any done comparing the economics of the  
3     patch, not the -- not the safety of the  
4     patch, the bioequivalency of the patches,  
5     patch to the -- to the OxyContin pill?

6           A.     Could you -- I'm sorry, I'm  
7     not understanding. When you say the  
8     economics, you are talking about the  
9     street value?

10          Q.     Oh, no, I'm not. I'm sorry.

11          A.     Okay.

12          Q.     We talked yesterday, there  
13     was -- we saw some studies between using  
14     OxyContin versus a fentanyl patch, and  
15     the -- and the effectiveness over time  
16     and how much it would cost, the economics  
17     of one pain treatment versus another.

18          A.     Okay.

19          Q.     Do you know -- so, I think  
20     you've told me there were no studies  
21     between the OxyContin -- between  
22     OxyContin pills or whatever, and any  
23     Janssen products with respect to safety  
24     or diversion; is that correct?

1           A.       With respect to diversion,  
2       we had studies that compared OxyContin  
3       and fentanyl, FEN-USA-71 and 72. So we  
4       had safety data. But not data with  
5       respect to misuse, abuse and diversion.  
6       Those data were available to us through  
7       the surveillance mechanisms that we had  
8       in place.

9           Q.       Do you know if Janssen ever  
10      conducted economic studies, and I'm  
11      talking about maybe the value to a  
12      formulary, or the value to a particular  
13      patient population that compared  
14      OxyContin to a matrix patch, you know,  
15      made by Janssen?

16          A.       And that would be after  
17      2009, so my answer would be no.

18          Q.       You are not -- you -- at  
19      least you're not aware from 2009 to 2011?

20          A.       That's correct.

21          Q.       And do you know, are you  
22      aware of anything, have you heard  
23      anything after 2011?

24          A.       No, I haven't.

1 Q. You can put that one away.

2 (Document marked for  
3 identification as Exhibit  
4 Janssen-Moskovitz-24)

5 BY MS. CONROY:

6 Q. The next exhibit is the  
7 Citizen's Petition, Exhibit 24. That is  
8 JAN-MS-02508937 through 48.

9 And you've -- you've talked  
10 about the Citizen's Petition a bit today.  
11 Is this the actual document?

12 A. Yes.

13 Q. And -- and ALZA filed the  
14 Citizen's Petition?

15 A. Yes.

16 Q. And although -- was -- ALZA  
17 was a part of Janssen at this time,  
18 November 12, 2004?

19 A. ALZA continued to  
20 manufacture the Duragesic reservoir and  
21 Janssen was responsible for sales and  
22 marketing. I don't recall the exact  
23 companywide relationship between the two.  
24 They continued to manufacture, sales and

1 marketing was the responsibility of  
2 Janssen.

3 Q. Is it fair to say that if  
4 Janssen had not wanted the Citizen's  
5 Petition to be filed, they could have  
6 stopped it?

7 A. Yes.

8 Q. And can you describe for me  
9 what a Citizen's Petition is?

10 A. A Citizen's Petition gives  
11 the opportunity for any interested party  
12 in submitting a request to the FDA based  
13 upon data that asks the FDA to take  
14 certain actions. It may be changes in  
15 the labeling, it may be additional  
16 studies. It's asking the FDA to take  
17 action relative to a certain compound.

18 Q. And -- and what was being  
19 asked in this context was that the FDA  
20 would require anyone that was  
21 manufacturing a fentanyl matrix system to  
22 develop and implement a comprehensive  
23 risk minimization program. Do you see  
24 that?

1 A. Yes.

2 Q. Is that the same as -- as a  
3 risk management plan or -- or is a risk  
4 minimization program something different?

5 A. At -- at this time the FDA  
6 was on the road towards developing risk  
7 management plans, risk minimization and  
8 assessment plans. But plans that would  
9 be able to track known risks and assess  
10 the frequency with which they are seen.

11 Q. And then ALZA, Janssen, also  
12 requested that the FDA classify matrix  
13 and reservoir fentanyl transdermal system  
14 as well as products with and without  
15 rate-controlling membranes as different  
16 dosage forms that are not pharmaceutical  
17 equivalents. Do you see that?

18 A. Yes.

19 Q. And can you explain what was  
20 meant by requesting that the products not  
21 be pharmaceutical equivalents?

22 A. So in a comparator way, the  
23 FDA does not consider tablets and  
24 capsules to be pharmaceutically

1 equivalent, even if they deliver the same  
2 amount of the active drug over the same  
3 period of time.

4 So the FDA already had  
5 guidelines under which they might  
6 classify the two as being bioequivalent,  
7 but not pharmaceutically equivalent.  
8 That relates to interchangeability at the  
9 level of the pharmacy. In some states at  
10 the time, if you write for the active  
11 compound, then the -- the pharmacy can  
12 fill that with what the FDA would  
13 designate as pharmaceutically equivalent.

14 So going back to my  
15 original, if you wrote for a capsule, you  
16 could not substitute a tablet.

17 Q. And so you were asking the  
18 FDA that if -- if a physician prescribed  
19 a reservoir matrix, that that would not  
20 be able to be --

21 A. That you couldn't -- that  
22 you couldn't fill that prescription with  
23 a fentanyl matrix patch.

24 Q. And in support of your

1 request, you see you talk about the  
2 differences in the abuse liability and  
3 drug delivery systems between the  
4 reservoir and the matrix, correct?

5 A. Yes. There are the outcome  
6 of the data that we generated over the  
7 previous year and a half.

8 Q. And what happened with the  
9 Citizen's Petition?

10 A. Well, the FDA took it under  
11 advisement. Ultimately they -- they  
12 rejected the Citizen's Petition.

13 Q. And after that rejection,  
14 Janssen then moved for an approval of a  
15 matrix formulation, matrix fentanyl  
16 delivery system formulation?

17 MR. LIFLAND: Object to the  
18 form of the question.

19 THE WITNESS: Yes, after.

20 But years later.

21 We continued to market the  
22 Duragesic as a reservoir fentanyl  
23 patch until 2009.

24 This was -- the rejection

1           came in January 2005. But we  
2           continued to market the reservoir  
3           patch through 2009 because of  
4           concerns over what we had brought  
5           forth in the studies that we did.

6       BY MS. CONROY:

7           Q.     And is the Citizen's  
8           Petition based on the data that was in  
9           the White Paper?

10          A.     Yes.

11          Q.     And in 2009 Janssen decided  
12          to go forward with the matrix formulation  
13          because of the review of the diversion  
14          data in the --

15          A.     All -- I'm sorry.

16          Q.     -- in the surveys?

17          A.     All of the surveillance  
18          data, that's correct.

19          Q.     Had you ever filed a  
20          Citizen's Petition prior to 2004 for any  
21          reason?

22          A.     Janssen had. I had not.

23          Q.     Had you ever done it  
24          subsequent to 2004?

1 A. No.

2 Q. You can put that away.

3 (Document marked for  
4 identification as Exhibit  
5 Janssen-Moskovitz-27.)

6 BY MS. CONROY:

7 Q. That is Exhibit 27. An  
8 e-mail from -- well the top e-mail is  
9 from you and it's dated March 24th of  
10 2008. And the Bates range is  
11 JAN-MS-02005184 to 185.

12 The subject is "The  
13 Duragesic Development Plan For a Matrix  
14 Patch." If you look at the bottom of  
15 the -- of Exhibit 27, the first page,  
16 there's an e-mail from Ravi Desiraju --

17 A. Desiraju.

18 Q. -- Desiraju. And who is  
19 that?

20 A. He was on -- I believe he  
21 was on the sales and marketing side or  
22 PGSM. He was not on the research side.

23 Q. Okay. And I see you are --  
24 you are one of the recipients.

1 A. Of Ravi Desiraju's e-mail.

2 Q. Correct. And I'm just  
3 looking at who else. Scott Trembley,  
4 he's in medical affairs at that point,  
5 correct?

6 A. No. He's on the sales and  
7 marketing side.

8 Q. Okay. Karen Naim, where is  
9 she from?

10 A. BRM is the benefit-risk  
11 management, U.S., so that was the safety  
12 group.

13 Q. Randolph, William Randolph,  
14 what's that group?

15 A. I believe that relates to  
16 the manufacturing. I'm not certain.  
17 It's not sales and marketing. It's not  
18 medical affairs.

19 Q. Okay. And Carolyn Gerhardt.  
20 What department is she in?

21 A. PRD would be the R&D side,  
22 the research and development side.

23 Q. And Donna Abbondanza?

24 A. I believe she was

1 regulatory. I'm not certain. But I  
2 believe she was regulatory.

3 Q. And Harindra Abeysinghe.  
4 She is after Carolyn Gerhardt.

5 A. That's a he. He was  
6 regulatory.

7 Q. Okay. Todd Moore.

8 A. Not certain.

9 Q. Okay. Henry Richards?

10 A. He was a physician, and I  
11 believe -- he had a variety of positions  
12 through the course of my time at Janssen.  
13 At times he reported to me. I believe at  
14 this time he looked at some of the safety  
15 issues. But I can't say that for  
16 certain.

17 Q. Okay. Did you say Ravi is a  
18 man, right?

19 A. Yes.

20 Q. So Mr. Desiraju, is he a  
21 physician or --

22 A. No. He is a pharmacist. I  
23 believe that's his background.

24 Q. He writes to the team, "As

1     you may know, during a teleconference  
2     with the FDA on Friday" -- and he's  
3     writing this e-mail on a Sunday -- "they  
4     strongly recommended that we proceed ASAP  
5     with the development and launch of a  
6     matrix formulation for Duragesic and  
7     replace the reservoir formulation with  
8     the matrix."

9                     Do you see that?

10                    A.     Yes.

11                    Q.     And he asked people to be  
12     ready to meet tomorrow to discuss the  
13     elements of a development plan, do you  
14     see that?

15                    A.     Yes.

16                    Q.     And then he also says he is  
17     going to check to see if some patches can  
18     be brought in from the EU and used in the  
19     United States.

20                    Do you see that?

21                    A.     Yes.

22                    Q.     Do you know if that ever  
23     happened?

24                    A.     I think that goes to what

1 I -- my recollection earlier, that to do  
2 the bioequivalency studies between the  
3 matrix that we were marketing in Europe  
4 and a matrix formulation that was being  
5 developed in the United States, that we  
6 wanted to have access to the European  
7 matrix so that we could do the  
8 bioequivalency studies to the matrix that  
9 would be produced in the United States.

10 Q. And I have -- I have your  
11 response to his e-mail, it looks like you  
12 kept the same folks on the e-mail chain  
13 to me.

14 A. Probably replied to all.

15 Q. Yeah. And it looks like you  
16 responded the next -- on Monday  
17 afternoon, but before the call that was  
18 scheduled.

19 A. Yes.

20 Q. And you clarify, "The FDA  
21 did not 'strongly recommend that we  
22 proceed ASAP with the development and  
23 launch of a matrix formulation for  
24 Duragesic and replace the reservoir

1 formulation with the matrix.'" "

2 And then you said, "If that  
3 were the case there would be no need for  
4 RADARS to update the report and for us to  
5 review the findings."

6 What did you mean by that?

7 A. So our concerns that we  
8 expressed in the Citizen's Petition based  
9 upon the studies that were conducted in  
10 late 2003, 2004 always remained, which is  
11 why we continued to manufacture the  
12 Duragesic reservoir.

13 We understood that because  
14 of the manufacturing issues with the  
15 Duragesic reservoir, the FDA expressed  
16 that they would like us to consider  
17 moving to a matrix formulation.

18 But my point in this was  
19 that while they -- while that was their  
20 preference and they wanted us to move to  
21 it, we would need to resolve the issue in  
22 our own minds whether the concerns we had  
23 expressed in the Citizen's Petition  
24 remained the case, whether there were

1 instances -- whether there were  
2 differences between the matrix  
3 formulation and our reservoir formulation  
4 with respect to potential for abuse,  
5 misuse and diversion.

6 Q. And now it's March of 2008.  
7 So you still expressed the same concerns  
8 that you had in the Citizen's Petition  
9 four years later?

10 A. Well we -- we didn't -- we  
11 didn't have data that would allay those  
12 concerns at this time.

13 Q. You didn't have the data or  
14 you didn't look at the data?

15 A. We didn't evaluate the data  
16 in a consistent manner that compared the  
17 two.

18 Q. So from the time that you  
19 filed the Citizen's Petition in November  
20 of 2004 until March of 2008, you had not  
21 gone back to the data that you had  
22 available to look to see whether or not  
23 there was diversion of either the  
24 reservoir matrix or the -- the reservoir

1 or the matrix?

2 MR. LIFLAND: Object to the  
3 form of the question.

4 THE WITNESS: I wouldn't  
5 characterize -- we reported in our  
6 surveillance programs any  
7 surveillance program that reported  
8 on abuse, misuse, diversion of all  
9 fentanyl products, and where  
10 possible, we had data for a matrix  
11 patch versus the reservoir patch.

12 We didn't do a comprehensive  
13 analysis of the differences  
14 between the two. We reported on  
15 the findings from our surveillance  
16 programs.

17 BY MS. CONROY:

18 Q. But you hadn't evaluated the  
19 difference between the reservoir patch  
20 diversion versus the matrix patch  
21 diversion?

22 A. We reported rates throughout  
23 this period.

24 Q. But -- but you had -- you

1 weren't comparing them, one patch to the  
2 other?

3 A. There -- that would be  
4 correct, we weren't consistently making a  
5 comparison, we were simply reporting the  
6 rates. Our focus was on our product.  
7 Our focus was on the Duragesic reservoir  
8 patch.

9 Q. Which was the subject of the  
10 sales training program that we looked at,  
11 that was the -- that was the discussion  
12 of the differences between the product  
13 that Janssen was selling, the reservoir  
14 patch, and the matrix patch being sold by  
15 Mylan?

16 MR. LIFLAND: Object to the  
17 form of the question.

18 THE WITNESS: So the sales  
19 training was to make the  
20 representatives aware that there  
21 was another formulation of the  
22 fentanyl patch that would be  
23 coming to market. It had nothing  
24 to do with any data about

1 comparison between the two.

2 BY MS. CONROY:

3 Q. It -- that --

4 A. There were no data at the  
5 time on rates of abuse, misuse and  
6 diversion that we could even refer to.  
7 These were all hypothetical issues in  
8 2004.

9 Q. Correct. But you did  
10 compare the reservoir patch to the matrix  
11 patch and you cited particular situations  
12 that could occur with the matrix patch  
13 that couldn't occur with the reservoir  
14 patch?

15 A. We cited --

16 MR. LIFLAND: Object to the  
17 form of the question.

18 THE WITNESS: We cited  
19 concerns based upon the data that  
20 we generated between 2003 and 2004  
21 that might occur with the  
22 introduce -- introduction of a new  
23 matrix patch to the market.

24 BY MS. CONROY:

1           Q.       And -- and Janssen had  
2       available to it data that it could have  
3       evaluated to determine what was happening  
4       in the market between the reservoir patch  
5       and the matrix patch, the differences,  
6       the comparison with respect to diversion,  
7       at least up until March of 2008 that it  
8       did not evaluate?

9           MR. LIFLAND:   Object to the  
10       form of the question.

11          THE WITNESS:   I wouldn't  
12       characterize it as did not  
13       evaluate.   We -- we were aware of  
14       all the data.   We were aware of  
15       rates of abuse, misuse, and  
16       diversion for all of the scheduled  
17       products that were reported in the  
18       surveillance systems.   We didn't  
19       do a consistent evaluation to --  
20       to reach a conclusion, were there  
21       differences in the rates of abuse,  
22       misuse and diversion.   We reported  
23       those rates on a consistent basis  
24       as part of our commitment to the

1 risk management program and the  
2 surveillance programs.

3 BY MS. CONROY:

4 Q. I understand that. But you  
5 were not reporting an evaluation of the  
6 differences between diversion of the  
7 reservoir versus the matrix, you were  
8 just reporting the diversion of any type  
9 of patch with fentanyl in it?

10 A. And conclusions in those  
11 reports that the rates of abuse, misuse  
12 and diversion of all pharmaceutical grade  
13 fentanyl products was low compared to  
14 other opioids.

15 But your characterization is  
16 correct, we didn't do a consistent look  
17 at the matrix patch versus the reservoir  
18 patch until this time in response to the  
19 FDA's request that we consider switching  
20 from the reservoir patch to the matrix  
21 patch.

22 Q. But the sales force did have  
23 information at this time about the  
24 differences between the reservoir patch

1 and the matrix patch with respect to  
2 abuse and diversion?

3 MR. LIFLAND: Object to the  
4 form of the question.

5 THE WITNESS: No, the sales  
6 force did not have access to the  
7 surveillance data that we  
8 generated over the period of time  
9 from 2005 to 2009.

10 If you're referring back to  
11 the 2004 sales training, we  
12 educated them on the physical  
13 properties of the -- the two  
14 formulations. And, based upon the  
15 physical properties, what might  
16 occur in a hypothetical case,  
17 based upon the data we generated  
18 over a period of time.

19 And that was the basis of  
20 the Citizen's Petition too.

21 BY MS. CONROY:

22 Q. Correct. But the sale --  
23 there -- there was nothing that went out  
24 to the sales force for example, in 2007

1 or 2008 that said, "Our thinking about  
2 this has changed."

3 There were -- the sales  
4 training was still that there were  
5 differences with respect to abuse and  
6 diversion between the reservoir patch and  
7 the matrix patch.

8 MR. LIFLAND: Object to the  
9 form of the question.

10 THE WITNESS: Well, we -- we  
11 did not share surveillance data  
12 with the sales force. We -- we  
13 educated the sales force in 2004  
14 because there was a new  
15 formulation coming to market.  
16 They couldn't promote regardless.

17 So they continued to be  
18 aware that there were other  
19 formulations of pharmaceutical  
20 grade fentanyl, fentanyl patches  
21 on the market, but we didn't share  
22 surveillance data with them. They  
23 did not know rates of abuse,  
24 misuse and diversion. Those were

1 reported directly to the FDA.

2 BY MS. CONROY:

3 Q. Well, they could promote the  
4 reservoir patch during that period,  
5 from --

6 MR. LIFLAND: Objection.

7 BY MS. CONROY:

8 Q. -- 2004 through 2009 when it  
9 was no longer available?

10 MR. LIFLAND: Object to the  
11 form of the question.

12 THE WITNESS: They would  
13 promote Duragesic based upon  
14 approved promotional materials.

15 Given the package insert  
16 and -- and all of the promotional  
17 materials on the appropriate  
18 selection, dose selection,  
19 monitoring and the patient  
20 education.

21 BY MS. CONROY:

22 Q. And you don't know as you  
23 sit here today whether there are  
24 promotional -- approved promotional

1 materials that compare the matrix patch,  
2 the technology of the matrix patch, to  
3 the reservoir patch?

4 A. I don't know.

5 Q. It says here, "The FDA made  
6 clear they would not allow for another  
7 recall of the type we had in 2004 and  
8 earlier this year."

9 I think we spoke about that  
10 earlier today. They were -- there were  
11 two recalls for leakage in the Duragesic  
12 patch, one in 2004, and one maybe January  
13 of 2008?

14 A. It was in that time frame.  
15 I don't recall the exact dates.

16 Q. And then you tell  
17 Mr. Desiraju that the -- that "while FDA  
18 indicated they would urge we move to an  
19 alternative formulation." And then you  
20 put in parentheses, "Matrix being the  
21 only viable option at the moment," but  
22 "the FDA was open to learning more about  
23 our decisions in 2004" -- and in -- "and  
24 in 2000 and 2004 to remain with the

1     reservoir and to review data that we will  
2     submit for abuse and diversion of the  
3     reservoir and the matrix."

4                     Do you see that?

5             A.     Yes.

6             Q.     And that's what you're  
7     talking about, then you -- at this point  
8     in March of 2008, you are indicating that  
9     it's time now to go back and take a  
10    closer look at the surveillance data?

11            A.     Well, certainly at this  
12    point we had three years of data so that  
13    we could also determine trends. Exactly  
14    right. We -- we had concerns throughout  
15    this period of time based upon the data  
16    we generated in 2003 and 2004, and we  
17    understood that the FDA was concerned  
18    about the manufacturing issues with the  
19    Duragesic reservoir and were open to  
20    moving to a matrix patch, but only after  
21    we satisfied ourselves and satisfied the  
22    FDA that the concerns we raised in the  
23    Citizen's Petition did not come to  
24    fruition, that we were not seeing an

1 increased signal for abuse, misuse,  
2 diversion in public safety with the  
3 matrix patch.

4 The FDA agreed with us on  
5 that. They allowed us to do the analysis  
6 of the surveillance data and submit that.

7 Q. And -- and that's what you  
8 were telling Mr. Desiraju, don't be --  
9 don't be so hasty, we still have work to  
10 do here?

11 A. I'd agree with that in a  
12 nutshell, yes.

13 Q. And do you know how the  
14 reservoir, the Duragesic reservoir was  
15 doing on the market as compared to the  
16 Mylan patch at that time?

17 A. Those data were shared in  
18 meetings. I couldn't give you the exact  
19 numbers. As is typical, when a generic  
20 is introduced to the market, the total  
21 number of prescriptions -- I'm not  
22 talking about sales -- the total number  
23 of prescriptions would increase for  
24 the -- for the matrix relative to the

1 branded product. And that was my  
2 understanding of what was happening  
3 with -- with generic formulations,  
4 because at this time there was more than  
5 one generic formulation on the market  
6 relative to the Duragesic reservoir  
7 patch.

8 Q. And -- and at this time,  
9 depending on a patient's health  
10 insurance, I guess, they could be -- a  
11 patient might receive a matrix  
12 formulation even if their physician had  
13 prescribed a reservoir formulation?

14 A. I believe that that would  
15 depend upon a patient's health insurance  
16 and regulations within the state. There  
17 are some states that allow  
18 interchangeability even if a physician  
19 writes for a branded product. I believe  
20 there are some states that don't allow  
21 that.

22 MS. CONROY: I think it's a  
23 good time for a lunch break.

24 MR. LIFLAND: Okay.

1 MS. CONROY: We can go off  
2 the record.

3 THE VIDEOGRAPHER: Stand by,  
4 please. The time is 12:56 p.m.  
5 Going off the record.

6 - - -  
7 (Lunch break.)

8 - - -  
9 THE VIDEOGRAPHER: The time  
10 is 2:18 p.m. Back on the record.

11 - - -  
12 A F T E R N O O N S E S S I O N

13 - - -  
14 EXAMINATION (Cont'd.)

15 - - -

16 BY MS. CONROY:

17 Q. Mr. Moskovitz, let me pass  
18 to you Exhibits 28 and 29.

19 (Document marked for  
20 identification as Exhibit  
21 Janssen-Moskovitz-28.)

22 (Document marked for  
23 identification as Exhibit  
24 Janssen-Moskovitz-29.)

1 BY MS. CONROY:

2 Q. We'll look at 28 first.

3 Exhibit 28 is what appears to be another  
4 slide deck dated April 20, 2007. The  
5 Bates number is, on the final page,  
6 JAN-MS-02305132. And this -- it's called  
7 the Duragesic Risk Management Overview.

8 Do you see that?

9 A. I do.

10 Q. And did you prepare this  
11 slide deck?

12 A. I ultimately presented the  
13 slide deck. I probably had assistance in  
14 preparing it.

15 Q. If you just would turn to --  
16 you know something, I don't -- some of  
17 them have -- this one does not have page  
18 numbers.

19 If you go to the very end  
20 and you go in a few slides, and I'm going  
21 to show you what I'm looking for. It's a  
22 map. Go in three -- about four slides.  
23 Yeah, that's it.

24 A. Okay.

1           Q.     I don't need -- if you need  
2     to refer to some other section of the  
3     slide deck, that's fine. But do I  
4     understand correctly that this was an  
5     indication that you could look at abuse  
6     and diversion down to a zip code area?

7           A.     Even without looking at  
8     this, in a general sense we tried to look  
9     at issues of abuse and diversion down to  
10    the zip code level.

11          Q.     Okay. And is that what that  
12    is showing, a zip code level? I think I  
13    read that somewhere else in the slide  
14    deck. I'm going to look for it here.  
15    But I see the three -- it's really hard  
16    to read.

17                   But do you see there are  
18    three numbers in this area of Eastern  
19    Kentucky, right on the border of West  
20    Virginia, and it looks like you have a  
21    412, 413, 414, that are in the center of  
22    those different pink color areas?

23          A.     Yes. And the -- on the side  
24    it says rates per three-digit zip code.

1 MR. LIFLAND: Could you  
2 pause for one second, because I'm  
3 having trouble finding the page.

4 MS. CONROY: Okay. Go to  
5 the very end, probably easy --

6 MR. LIFLAND: And I just --  
7 I would tell the witness, if you  
8 would like to just flip through,  
9 just so you understand the context  
10 of all of this, feel free. But  
11 it's up to you.

12 THE WITNESS: Yeah, just in  
13 terms of this map, it looks like  
14 we're reporting on a three-digit  
15 zip code basis.

16 BY MS. CONROY:

17 Q. And is that data that's  
18 available to Janssen from the RADARS  
19 system from the Poison Control Centers,  
20 if you know?

21 A. Based upon some of the  
22 slides. Prior to that, that would be my  
23 best assessment, yes.

24 Q. Have you yourself ever honed

1 in on a particular zip code or area of  
2 the country with respect to data  
3 concerning the Duragesic patch?

4 A. Could you clarify what you  
5 mean by honed in? I would get the data.  
6 Occasionally the data would indicate that  
7 there were particular concerns coming  
8 from one aspect of the surveillance data  
9 that affected a certain three-digit zip  
10 code. And that they might have made a  
11 decision to do more intensive  
12 surveillance at of area. So I am not  
13 sure what you mean by honed in.

14 So I was aware that there  
15 were three-digit ZIP codes that came up  
16 on the surveillance issue as areas of  
17 concern.

18 Q. Did you -- let me ask it  
19 this way. Was that something that you  
20 would look at, you might identify a  
21 three-digit zip code area and then you  
22 would ask for an investigator to go and  
23 look or do some other action, or is it  
24 something that you were aware of

1     happening but you were not the person who  
2     was actually saying, "Hey, you better go  
3     look at a particular area"?

4             A.     That second, right. I would  
5     receive the report and they would  
6     indicate where there were some findings.  
7     And so I was aware of the reports. I  
8     would not then tell them what to do.

9             Q.     Okay. Do you know if those  
10    reports, if it was possible, for example,  
11    here, to identify a particular  
12    three-digit zip code area where there  
13    were issues? Do you know if it was  
14    possible then to compare that to IMS  
15    data, prescription data with respect to  
16    that zip code area?

17            A.     I don't know if it could be  
18    done at a zip code level. And I -- so  
19    what they're seeing here are issues of  
20    abuse, misuse, and diversion. To begin  
21    with, it wouldn't necessarily mean that  
22    it was Duragesic or pharmaceutical grade  
23    fentanyl or any branded product of  
24    fentanyl. But -- so I don't think it

1       could be done.

2               Q.       You don't think that if  
3       there was an investigator that was going  
4       to go out and look at reports of misuse  
5       in a three-digit zip code area that was  
6       determined from RADARS, you don't think  
7       it would be possible to look at  
8       prescription data for that same area  
9       through IMS?

10              A.       Well, I suspect that you  
11       could look at physicians who were  
12       operating in that three-digit zip code  
13       and look at the prescriptions for that  
14       three-digit zip code.

15              Q.       I'm not suggesting it would  
16       be -- it would be linked. I'm just  
17       asking if it could be done.

18              A.       Right. Yeah, I see where  
19       you're going with it. I believe that the  
20       IMS data could go down to the granularity  
21       of a three-digit zip code.

22              Q.       Do you know if the IMS data  
23       that was available to Janssen could look  
24       at where a prescription was filled as

1       opposed to the physician who prescribed  
2       it? Do you know one way or the other?

3               A.       I don't.

4               Q.       As far as you understand it,  
5       that RADARS data, you can't distinguish  
6       between patient misuse and abuse,  
7       nonpatient misuse and abuse, physician  
8       misuse or abuse, or pharmacy misuse or  
9       abuse in the RADARS data?

10              A.       Well, there were different  
11       streams within the RADARS data. In some  
12       cases, key informant network may define  
13       what the abuse was, that there was a  
14       diversion of something or that there was  
15       laboratory data of fentanyl found in a  
16       laboratory examination of a death case  
17       for example.

18                      So we would know from some  
19       streams that it was fentanyl, from other  
20       streams the key informant network and  
21       the -- and we had police data. They  
22       might state in the police data that it  
23       was a branded product or that it was  
24       simply fentanyl.

1 Q. Could you determine a  
2 distinction among those physician --  
3 abuse issues, or patients or pharmacy in  
4 DAWN data?

5 A. I -- my understanding is the  
6 DAWN data were fentanyl mentions. So you  
7 could not distinguish it in the DAWN  
8 data.

9 Q. What about in the poison  
10 center control (sic) data?

11 A. At times we could  
12 distinguish it, but not consistently.

13 Q. Would it be fair to say that  
14 for SCEPTRE data, it would totally depend  
15 on what you were told about it?

16 A. So for SCEPTRE data there  
17 was always an attempt to try to -- to try  
18 to get as much information about a  
19 reported case as possible. If there were  
20 issues that were unresolved in the  
21 initial report, there might be an inquiry  
22 to the reporter to try to get additional  
23 information. Sometimes we would get  
24 that; sometimes we wouldn't.

1           Q.     Take a look at the next  
2     exhibit, which is Exhibit 29. And  
3     Exhibit 29 is a cover e-mail from you to  
4     Fatih Sarioz. No idea how to pronounce  
5     that. I'm sure I've pronounced it  
6     incorrectly. I just don't know how --

7           A.     I can't do better.

8           Q.     Man or woman? Do you know?

9           A.     No, I don't.

10          Q.     Whoever this is, is it  
11     Janssen in Turkey?

12          A.     Yeah. Just going down to  
13     the message down at the very bottom of  
14     that. It says, "Let me introduce myself.  
15     I am" -- and I'm assuming health  
16     economics manager of Janssen Turkey.

17          Q.     And this person sent this  
18     e-mail to you on August 7th of 2008. He  
19     or she says, "In Turkey, the opioid  
20     market is very small because MOH has the  
21     concerns about the abuse potential of  
22     these products. According to our growth  
23     plan, we are planning to be a partner of  
24     MOH and show them the need of the

1 patients to these products and  
2 desensitize them by showing evidence that  
3 Duragesic has no/limited abuse  
4 potential."

5 Do you see that?

6 A. I do.

7 Q. And so she was asking you if  
8 you could give her some information,  
9 that's on the next page, about your  
10 project.

11 Do you see that?

12 A. Yes.

13 Q. And then you respond and  
14 say, "It would be incorrect to say that  
15 there's a risk management plan for  
16 Duragesic in the U.S. to show that  
17 Duragesic has not been abused. Rather,  
18 we recognize that fentanyl is attractive  
19 as a drug of abuse; and, therefore, for  
20 Duragesic, there are significant risks  
21 for diversion and abuse, as well as  
22 misuse (including off-label uses) and  
23 overdose." And then --

24 Did I read that correctly?

1 A. Yes.

2 Q. And then you attach the risk  
3 management plan that outlines various  
4 risks and provides risk mitigation  
5 strategies, including educational  
6 activities and surveillance to monitor  
7 for diversion, abuse, and misuse thereby  
8 maintaining a favorable benefit-to-risk  
9 ratio.

10 The benefit-to-risk ratio,  
11 you're -- you are talking about a  
12 favorable benefit to risk ratio of the  
13 marketing and sale of Duragesic, correct?

14 A. The continued marketing  
15 availability, that the benefits of using  
16 Duragesic appropriately, which includes  
17 proper patient selection, proper dose  
18 selection, proper monitoring, proper  
19 patient education, would outweigh the  
20 risks associated with the use of the  
21 drug.

22 Q. And then if you turn to the  
23 actual revised risk management plan that  
24 is dated June 14th of 2007.

1 Do you see that?

2 A. Yes.

3 Q. And were you involved in the  
4 preparation of the risk -- of the revised  
5 risk management plan?

6 A. Involved, yes.

7 Q. Okay. How involved were  
8 you?

9 A. Well, we were certainly  
10 aware of the various streams of data that  
11 would be coming in around the risk  
12 management plan. We probably held the  
13 budget that would fund the various groups  
14 that were providing us with those data  
15 streams. We would have them come in, we  
16 would evaluate them, along with the  
17 safety group and other groups within the  
18 company and make sure that it was  
19 adequate to meet the needs of the Food  
20 and Drug Administration as well.

21 Q. Would the document itself,  
22 as you were working on it, reside in  
23 medical affairs?

24 A. I don't recall whether the

1 document ultimately resided in medical  
2 affairs. But I know ultimately there was  
3 a separate benefit/risk group that had  
4 overall responsibility for the REMS  
5 program and later the RADARS program.  
6 And they assumed responsibility for it.  
7 It certainly started off within our  
8 group, but I -- it involved the safety  
9 group and other groups. So I don't know  
10 how I would answer the question where it  
11 resided. It -- I mean, it was generally  
12 available to all those groups, including  
13 the regulatory group obviously.

14 Q. Would you --

15 A. I -- I might answer that by  
16 saying, since the regulatory group was  
17 the direct interface with the Food and  
18 Drug Administration, the final document  
19 would probably reside with regulatory.

20 Q. Would -- would there be a  
21 final document without your review of the  
22 entire document?

23 A. No.

24 Q. And it -- but it would also

1 be fair to say that there are sections  
2 that other people other than you would  
3 have contributed to?

4 A. Absolutely correct.

5 Q. But you would have read all  
6 of it?

7 A. I would have read all -- all  
8 of it and been aware of it.

9 Q. If you could turn to  
10 Page 39. Oh, this is -- did I explain --  
11 this is JAN-MS-01204900. And it's an --  
12 it's the attachment to the e-mail which  
13 is the front page, which is  
14 JAN-MS-01204898.

15 I see here in the first full  
16 paragraph a reference to iatrogenic  
17 addiction, and then it says, "It's" --  
18 "it's addiction that occurs as a result  
19 of treatment by a physician."

20 I don't think I had asked  
21 you previously for a definition for  
22 iatrogenic addiction. Do you agree with  
23 that definition?

24 A. I do. It's generally

1       accepted.

2               Q.       And is there -- we don't see  
3       that term very often or I have not seen  
4       it very often in the documents. We  
5       didn't see it in the White Paper for  
6       example. What -- is there a reason why  
7       the term "iatrogenic addiction" is used  
8       in the risk management plan?

9               A.       It was one of the identified  
10       risks of opioids.

11              Q.       Is it different than  
12       addiction, a risk of addiction?

13              A.       It -- it leads to the same  
14       outcome. There is a patient who becomes  
15       addicted to the drug. Iatrogenic would  
16       be that it's the result of treatment by a  
17       physician.

18                      A patient may become  
19       addicted to opioids that he or she might  
20       have obtained illicitly, not through a  
21       physician, and that would not be an  
22       instance of iatrogenic addiction.

23              Q.       Is there any -- so would it  
24       be fair to say that the iatrogenic is how

1 someone becomes addicted? But the  
2 addiction is the same whether they  
3 received a prescription from a physician  
4 or they got it on the street, if there's  
5 a diagnosis of addiction?

6 A. I would say that the source  
7 of the opioids would be through a  
8 physician prescription rather than  
9 through some other channel.

10 Q. And -- and where you --  
11 where someone got the opioids would not  
12 change once they were addicted, the  
13 symptoms of the condition of addiction  
14 would be the same, correct?

15 A. Yes. That -- if it would  
16 meet the definition of addiction, which  
17 is to say destructive behaviors in -- in  
18 seeking drug, yes.

19 Q. If you could go to Page 52,  
20 please. You see there's a -- the second  
21 paragraph on the page says, "In summary,  
22 there's more than a decade of commercial  
23 experience with transdermal fentanyl as a  
24 mainstay of pain management. The

1 physical characteristics of the system  
2 that provide gradual onset of effect and  
3 steady pain relief also render a properly  
4 used and disposed system relatively  
5 unattractive to those seeking to obtain  
6 drug 'highs' or euphoria."

7 Do you see that?

8 A. Yes.

9 Q. At this time, the date of  
10 this document which is June 14th of 2007,  
11 had Janssen performed any studies to  
12 determine whether or not a transdermal  
13 system would be unattractive to persons  
14 seeking to obtain drug highs or euphoria?

15 MR. LIFLAND: Object to the  
16 form of the question.

17 THE WITNESS: I would  
18 consider the streams of the RADARS  
19 program, the risk management  
20 program, the surveillance program,  
21 to be studies, but not in the  
22 sense of controlled clinical  
23 trials. If -- if that's what  
24 you're asking about.

1 BY MS. CONROY:

2 Q. So, the -- I -- well, let me  
3 ask it this way. Is your answer then  
4 that the support for this statement that  
5 the physical characteristics of the  
6 transdermal statement -- system are  
7 unattractive to people seeking drug highs  
8 or euphoria, are RADARS and other  
9 surveillance mechanisms for systems?

10 MR. LIFLAND: Object to the  
11 form of the question. I think we  
12 need to quote it correctly. You  
13 left out the word "relatively."

14 MS. CONROY: Oh, I'm sorry.  
15 Let me -- let me start again.

16 BY MS. CONROY:

17 Q. Well, let me just ask you.  
18 What is your support of the first two  
19 sentences of that paragraph?

20 A. We had the DAWN data, we had  
21 other streams of data coming in through  
22 the risk management plan, surveillance.  
23 We had data from longer term clinical  
24 trials where we looked at adverse events,

1 and as part of the adverse events, there  
2 would also be reports of abuse, misuse,  
3 addiction, euphoria. We always saw those  
4 to be low when -- in -- in those clinical  
5 trials.

6 So we felt confident that by  
7 virtue of the delivery system and the  
8 information that we were collecting,  
9 including some published information  
10 about retrospective data on patients who  
11 had been treated long-term with a whole  
12 variety of Schedule II opioids,  
13 long-acting opioids, that the abuse  
14 potential or the attractiveness of the  
15 reservoir system relative to other  
16 formulations that were out there, other  
17 drugs that were out there were -- it was  
18 relatively unattractive.

19 Q. Had you ever done a study  
20 that had a primary endpoint to determine  
21 whether the reservoir transdermal system  
22 would be unattractive to those seeking --  
23 relatively unattractive to those seeking  
24 to obtain drug highs or euphoria?

1           A.       Well, the -- one of the  
2       studies that was done in conjunction with  
3       the data filed with the Citizen's  
4       Petition looked at attractiveness of the  
5       fentanyl -- the Duragesic transdermal  
6       fentanyl system with other Schedule II  
7       opioids. And, in fact, on that scale, we  
8       saw that Duragesic was the lowest, or  
9       among the lowest with respect to  
10      attractiveness, relative to the other  
11      opioids.

12           Q.       Was that with respect to  
13      obtaining a high or euphoria?

14           A.       No, it was -- attractiveness  
15      was the endpoint.

16           Q.       Right. Other --

17           A.       It didn't actually take the  
18      drugs.

19           Q.       Right. Well, we saw that  
20      there was -- at least at one time we saw  
21      that there was a proposed study that was  
22      not actually done that would determine  
23      when someone was chewing a patch whether  
24      or not there was a difference between the

1 high or the euphoria between the  
2 reservoir and the matrix, correct?

3 A. Correct.

4 Q. That was not done, correct?

5 A. Correct.

6 Q. So are you aware of any  
7 other study that was done with a primary  
8 endpoint of determining the relative  
9 unattractiveness of obtaining a drug high  
10 or euphoria from a reservoir patch?

11 A. Where the endpoint was  
12 getting a high, not just hoping to.

13 Q. Doctor, what it says here,  
14 "unattractive" -- "relatively  
15 unattractive to those seeking to obtain  
16 drug highs or euphoria." Is there any  
17 study that the primary endpoint was that?

18 A. Well, I would posit that the  
19 attractiveness scale did measure  
20 attractiveness because -- these drugs  
21 were attractive because they were looking  
22 to get a high. If they wouldn't get a  
23 high, the -- the drugs would not be  
24 attractive to them.

1                   So if you would, the -- that  
2                   would be a surrogate measure of a high.  
3                   The attractiveness of the drug would be a  
4                   surrogate measure of obtaining a high.

5                   It wouldn't be attractive to  
6                   an individual if he or she didn't obtain  
7                   the high that he or she was looking for.

8                   Q.       I understand what you're  
9                   saying, and I believe that's when the  
10                  drug is misused and abused.

11                  This sentence suggests to me  
12                  that what's being explained is it's the  
13                  physical characteristics of the system  
14                  that provide gradual onset of effect and  
15                  steady pain relief also render a properly  
16                  used and disposed system relatively  
17                  unattractive to those seeking to obtain  
18                  drug highs or euphoria.

19                  So that suggests to me that  
20                  you're not looking at individuals who are  
21                  abusing, the way that test did?

22                  A.       That -- that test looked at  
23                  individuals who had a history of misuse,  
24                  abuse, and diversion, and what they found

1 attractive about these systems which  
2 included the Duragesic reservoir.

3 They found it attractive  
4 because they were seeking to use the  
5 systems to get a high. Yes, we measured  
6 attractiveness, but it -- I believe that  
7 the attractiveness is a surrogate measure  
8 of their ability to get euphoria.

9 Q. And -- and that's the -- and  
10 that's the study that is support for this  
11 statement?

12 A. That and the other streams  
13 of information about the lack of interest  
14 in obtaining Duragesic because the system  
15 was designed to release a -- a controlled  
16 amount of fentanyl over an extended  
17 period of time.

18 Q. And the FDA, however, at  
19 least in their rejection of the Citizen's  
20 Petition, did not agree that there was a  
21 lower abuse potential for the reservoir  
22 patch, correct?

23 A. The FDA didn't agree that --

24 MR. LIFLAND: I'm just going

1           to object to the form of the  
2           question.

3                       Sorry. Go ahead.

4                       THE WITNESS: The FDA didn't  
5           agree that the data that we  
6           submitted would require what we  
7           requested them to institute a risk  
8           management plan and a difference  
9           in -- of designating a reservoir  
10          patch and a matrix patch, because  
11          under conditions of use that were  
12          specified in the package insert,  
13          appropriate conditions of use, the  
14          two drugs delivered a  
15          bioequivalent amount of fentanyl  
16          through the skin.

17                      Clearly, the FDA has and  
18          continues to have concerns about  
19          abuse, misuse, and diversion. But  
20          their focus with respect to the  
21          Citizen's Petition was on the  
22          patient who is properly selected  
23          for whom the package insert is  
24          written, with the appropriate

1           warnings about any of the types of  
2           activities that might lead to the  
3           increased fentanyl release or  
4           potential increased release with  
5           heat or whatever. That's why they  
6           ultimately rejected the Citizen's  
7           Petition.

8       BY MS. CONROY:

9           Q.     If you could turn to Page  
10          109, please. Actually go back -- to make  
11          more sense, take a look at page 108, in  
12          the middle of the page where it says,  
13          "Additional measures for Duragesic."

14                 And it says, "To further  
15          mitigate the possibility of diversion of  
16          Duragesic, the following steps are  
17          taken." And then there's a number, if  
18          you go from page 108, take a look through  
19          page 109, 110, and actually through the  
20          rest -- there's only one more page left.

21                 It identifies ways to  
22          mitigate the diversion of Duragesic.

23                 Did you have anything to do  
24          with the collection of information for

1       this portion of the --

2               A.       No. This is clearly coming  
3       from the supply chain, and it describes  
4       the process of distribution for  
5       Duragesic.

6               Q.       And do you see, on Page 109  
7       it says under Number 4, "As per  
8       regulation, orders are monitored for  
9       suspicious quantities. Supply of product  
10      is stocked to any customers engaging in  
11      unlawful conduct or product diversion.

12                      "The mitigation measures  
13      serve to safeguard the integrity of the  
14      supply chain and to minimize the amount  
15      of product in distribution."

16                      Do you see that?

17               A.       I do.

18               Q.       Do you have any reason to  
19      disagree with that statement?

20               A.       I don't.

21               Q.       Okay. And then it goes on  
22      with subpart A, "The demand for Duragesic  
23      as quantified by IMS Health prescription  
24      data is matched with actual order

1 quantities to verify that the supply  
2 chain does not" -- "does not contain  
3 excess product."

4 Do you see that?

5 A. I do.

6 Q. Where at Janssen was that  
7 done? Do you know what department or  
8 division?

9 A. Again, I assume that this is  
10 all part of the supply chain and  
11 manufacturing.

12 Q. And if you look up above,  
13 there's a JOM in all caps, written there.  
14 Do you know what JOM is? Sorry --

15 A. Yeah, on B.

16 Q. Yeah, on B. There might be  
17 a reference earlier on the page. Let's  
18 see.

19 A. I believe -- this is 2007.  
20 I believe it's Janssen Ortho-McNeil.

21 Q. Janssen Ortho-McNeil?

22 A. Yes. So in 2004 the medical  
23 affairs groups within Janssen at  
24 Ortho-McNeil were brought together and

1 all of the pain products were  
2 consolidated under the Janssen  
3 Ortho-McNeil group.

4 Q. And Janssen Ortho-McNeil  
5 also would have been responsible for the  
6 monitoring of suspicious quantities and  
7 the integrity of the supply chain?

8 A. Yes, because at that time  
9 all of the activities were now within one  
10 company.

11 Q. I'm being shown a website  
12 for JOM Pharmaceutical Services, Inc.  
13 And it just -- it's just a JOM. Do you  
14 know if there's a different company now,  
15 JOM, that's not known as Janssen  
16 Ortho-McNeil?

17 A. There is no Janssen  
18 Ortho-McNeil today. At some point the --  
19 Johnson & Johnson consolidated the  
20 activities all under the name of Janssen.

21 Q. Do you know if -- you've  
22 been gone for a while. You may not know.  
23 Do you know if it's called JOM or J-O-M  
24 or how they refer to that company?

1           A.       I believe it's called  
2       Janssen Pharmaceuticals, a division of  
3       Johnson & Johnson.

4                   MR. LIFLAND:   May I clarify,  
5       just to look at page 108.

6                   MS. CONROY:    Sure.

7                   MR. LIFLAND:   There's a  
8       reference to --

9                   MS. CONROY:    Oh, did you  
10      find it?

11                  MR. LIFLAND:   It may be  
12      referring simply to the central  
13      distribution center that's  
14      referred to on 108.   But I don't  
15      know if the witness can speak to  
16      that.   I don't know if that's what  
17      the website is.

18                  MS. CONROY:    I don't -- my  
19      understanding -- I'm going to look  
20      a little further back.   My  
21      understanding is that it's not --  
22      well --

23                  THE WITNESS:   Well, under --  
24      at the -- I'm sorry.   At the

1 bottom of 108 it states, "Domestic  
2 shipments originate from the  
3 central distribution center in  
4 Somerset New Jersey (Janssen  
5 Ortho-McNeil)."

6 BY MS. CONROY:

7 Q. You found it.

8 A. So that's my assumption,  
9 that JOM is, in fact, Janssen  
10 Ortho-McNeil.

11 Q. Great. Thank you. Like  
12 every other company, they seem to go to  
13 the acronym after so many years.

14 A. And they appropriately did  
15 that after first writing it out. We just  
16 took a while to find the original full  
17 name.

18 Q. Yes. That's right. And if  
19 you could take a look on Page 110. The  
20 second bullet point says, "Authorized  
21 demand is defined as the calculated total  
22 demand for the past 52 weeks divided by  
23 the same number of weeks factored for  
24 both price change activity and product

1 growth rate as JOM and its affiliate  
2 companies deem appropriate."

3 Do you see that?

4 A. I do.

5 Q. Do -- have you ever seen any  
6 of these calculated -- these demand  
7 calculations?

8 A. I haven't seen them. But I  
9 was aware that as part of the  
10 responsibilities in manufacturing and  
11 marketing a scheduled product, that we  
12 would have to assess the need for raw  
13 product that would go into the production  
14 of finished product on a regular basis.

15 Q. And what about after the  
16 product was -- you had a final product  
17 and it was manufactured apparently from  
18 this. There was also supply integrity  
19 protocols with respect to how much  
20 finished product was going out the door,  
21 correct?

22 A. That's my understanding.

23 Q. Then the next bullet point  
24 says, "In the event that orders for any

1 specific product for any specific 'ship  
2 to' location significantly exceed the  
3 authorized demand for this product, JOM  
4 will contact the customer to review the  
5 order."

6 Do you see that?

7 A. I do.

8 Q. Were you ever in the chain  
9 of communication -- for example, were you  
10 ever told that there was a particular  
11 customer that had been informed that they  
12 had exceeded the order, for example?

13 A. No.

14 Q. As far as you know, that was  
15 a JOM responsibility?

16 A. Yes.

17 Q. And then a little bit  
18 further down on the page, it says,  
19 "Additionally, per request of the DEA,  
20 quarterly Duragesic sales analysis  
21 reports are submitted to the agency."

22 Do you see that?

23 A. I do.

24 Q. They're submitted to DEA,

1 correct?

2 A. Correct.

3 Q. "These reports detail  
4 manufacturing plant output from ALZA to  
5 Janssen Pharmaceutical, Inc." -- that's  
6 the manufacturing piece, right?

7 A. The finished product.

8 Q. -- "sales from Janssen to  
9 wholesalers, and IMS data on  
10 prescriptions filled by retail  
11 pharmacies, hospitals, and long-term care  
12 facilities."

13 Do you see that?

14 A. I do.

15 Q. And so would it be fair to  
16 say that all of that data was available  
17 to Janssen Ortho-McNeil in order to  
18 create reports for the DEA?

19 A. That's my understanding of  
20 what it states here.

21 MS. CONROY: That is all I  
22 have for now. I know that your  
23 counsel is going to ask you some  
24 questions as well. I bet you I'll

1 be back.

2 THE VIDEOGRAPHER: Shall we  
3 go off the record?

4 MR. LIFLAND: Yes, let's go  
5 off the record.

6 THE VIDEOGRAPHER: Okay.  
7 The time is 2:55 p.m. We are  
8 going off the record.

9 (Short break.)

10 THE VIDEOGRAPHER: We are  
11 back on the record. The time is  
12 3:18 p.m.

13 - - -

14 EXAMINATION

15 - - -

16 BY MR. LIFLAND:

17 Q. Good afternoon,  
18 Dr. Moskovitz?

19 A. Good afternoon.

20 MR. LIFLAND: I'd like to  
21 start, Counsel, just by following  
22 up a couple of areas from his  
23 30(b)(6) corporate designee  
24 testimony. So these will be given

1           initially as -- in his capacity as  
2           the corporate designee for Janssen  
3           on the topics that -- that were  
4           specified. And then once we're  
5           done with that, we can indicate on  
6           the record and proceed with a  
7           normal direct examination in his  
8           personal capacity.

9                       MS. CONROY: That's fine.

10                      MR. LIFLAND: Okay.

11 BY MR. LIFLAND:

12                      Q.     Dr. Moskovitz, one of the  
13           questions that you were asked yesterday  
14           was whether you knew whether the company  
15           continued to report progress reports  
16           under the risk management plan to the FDA  
17           after the last one that was marked as an  
18           exhibit which I believe was around 2012,  
19           and you responded that you didn't have  
20           that information.

21                            Have you had the opportunity  
22           since your dep -- the first part of your  
23           deposition yesterday to go back and see  
24           if you could find the information to

1 answer that question?

2 A. I have.

3 Q. Okay. Let me place before  
4 you a document which we'll mark as the  
5 next in order.

6 MR. LIFLAND: What number  
7 would that be? Ah, 30.

8 (Document marked for  
9 identification as Exhibit  
10 Janssen-Moskovitz-30.)

11 BY MR. LIFLAND:

12 Q. Can you tell me what that  
13 document is?

14 A. This is the risk evaluation  
15 mitigation strategy, the REMS program,  
16 that was prepared by what ultimately  
17 became the REMS programs company.

18 These are a group of opioid  
19 manufacturers that agreed to develop,  
20 with the FDA's guidance, a class-wide  
21 REMS that covered all of the long-acting  
22 opioid products.

23 Q. Can you turn to Page 20 of  
24 the document please. And before I --

1 before I go further, let me read the  
2 Bates number in. It's JAN-MS-00935481.  
3 And it goes through, it looks like,  
4 00935534.

5 Turning to Page 20, I'd like  
6 to draw your attention to Item 5. Can  
7 you tell me what that describes?

8 A. Just reading the,  
9 "Commitment to surveillance monitoring  
10 for misuse, abuse, overdose, addiction,  
11 death and any intervention to be taken  
12 resulting from signals of these metrics,"  
13 and I won't continue reading on.

14 So in essence, this was a  
15 commitment to continue the surveillance  
16 programs that -- as part of the  
17 consortium that we already had in place  
18 for Duragesic, but at this point, since  
19 it became a class-wide REMS, we would  
20 participate in the surveillance  
21 activities along with the consortium of  
22 the other companies.

23 Q. So it's your understanding  
24 that those surveillance activities

1 continued for Duragesic, but the  
2 reporting was then done through the REMS  
3 process?

4 A. That's correct.

5 (Document marked for  
6 identification as Exhibit  
7 Janssen-Moskovitz-31.)

8 BY MR. LIFLAND:

9 Q. Let me show you what I'll  
10 mark as Exhibit 31.

11 (Whereupon, a discussion was  
12 held off the stenographic record.)

13 BY MR. LIFLAND:

14 Q. Can you tell us what  
15 Exhibit 31 is?

16 A. This is a letter to the Food  
17 and Drug Administration that describes  
18 our transition from having the individual  
19 REMS program for Duragesic to now  
20 transitioning to the consortium-wide REMS  
21 program for all long-acting opioids. And  
22 the most important information here is,  
23 in reading it, "The company now  
24 transitions to the new REMS programs

1 activities as approved by the agency.  
2 This submission will serve as our final  
3 RMP" -- risk management program --  
4 "report, providing Duragesic risk  
5 management information in the format of  
6 our previously filed reports."

7 Q. All right. And just for the  
8 record, the Bates number on that is  
9 JAN-MS-00700680 through 81.

10 The second topic, you were  
11 asked yesterday in connection with your  
12 corporate witness testimony in your  
13 capacity as a corporate designee about  
14 whether the company, Janssen, and I think  
15 Johnson & Johnson may have been  
16 mentioned, has a fixed definition or a  
17 standard definition of the terms  
18 "dependence," the term "addiction."  
19 There may have been one other term.

20 Does -- do Janssen and  
21 Johnson & Johnson have fixed corporate  
22 definitions of those terms that apply  
23 whenever the terms are used in the  
24 company?

1                   A.       No.

2                   Q.       And how would you know, if  
3       you saw the term in a company document,  
4       what was meant if a term like  
5       "dependence" were used or a term like  
6       "addiction" was used?

7                   A.       I would have to look at the  
8       context in which it was used, by whom it  
9       was used. If you go through the  
10      literature there are a variety of  
11      definitions, specific definitions around  
12      each of those terms.

13                         If it came from a clinical  
14      report, a clinical trial, then they would  
15      define the criteria upon which they would  
16      use that definition. If it came from an  
17      observational study, they would indicate  
18      how they might have arrived at that  
19      definition.

20                         But there was no -- there  
21      certainly was no company definition that  
22      assured that there was consistent use of  
23      that terminology within the company.

24                   Q.       So, for example, it's

1 possible that in a company document, the  
2 company employee might simply use the  
3 term incorrectly?

4 A. Absolutely.

5 Q. So one would have to look at  
6 the context and then make a -- make a  
7 judgment as to how the term was being  
8 used?

9 A. That's correct.

10 MR. LIFLAND: That's all I  
11 had on the corporate witness  
12 testimony.

13 MS. CONROY: Okay.

14 BY MR. LIFLAND:

15 Q. Okay. Dr. Moskovitz, we're  
16 now going to turn to direct examination  
17 in your capacity as a fact witness.

18 I'd like to just briefly  
19 once again go over your background and  
20 credentials. We won't spend a lot of  
21 time on this. But just so we have a  
22 continuous testimony.

23 A. Okay.

24 Q. You're a medical doctor?

1 A. Yes.

2 Q. And where did you go to  
3 medical school?

4 A. Boston University.

5 Q. And what -- when did you  
6 graduate?

7 A. It was a combined six-year  
8 program. So I was at Boston University,  
9 undergraduate and medical school through  
10 1970, '76, and graduated in '76.

11 Q. Can you give us a capsule  
12 description of your areas of specialty  
13 and training?

14 A. Within medical school or  
15 subsequent?

16 Q. Medical school.

17 A. Okay. So it was a standard  
18 medical school training. We were trained  
19 in biology, physiology, pharmacology.  
20 The last two years were generally spent  
21 in doing clinical rotations on the  
22 various aspects of medicine with exposure  
23 to pediatrics, and OB/GYN, internal  
24 medicine, surgery, the emergency room,

1 and subspecialties that might interest  
2 us. And so we had a broad overview of  
3 the practice of medicine.

4 Q. And in connection with some  
5 of that work, for example, your emergency  
6 room experience, did you have any  
7 occasion to prescribe opioid pain  
8 products?

9 A. Yes. But my -- so beyond  
10 medical school, I did an internship and  
11 three years of residency, and two years  
12 of fellowship. And that's where the bulk  
13 of my direct patient care comes in. And  
14 certainly through the period of time that  
15 I was an intern, resident, and fellow, I  
16 had opportunities to prescribe opioids.

17 Q. And after medical school,  
18 what did you go on to do?

19 A. I did training in internal  
20 medicine and subsequently in the  
21 subspecialty of infectious disease.

22 Q. And when you went to work,  
23 what did you do after that?

24 A. After I finished my

1 fellowship in infectious diseases, I went  
2 to work for Hoffman-La Roche.

3 Q. And that's a pharmaceutical  
4 company?

5 A. Yes. In Nutley, New Jersey.

6 Q. And you worked in the area  
7 of the pharmaceutical development?

8 A. I worked on the research and  
9 development side with anti-infectives.

10 Q. And would that have given  
11 you experience with clinical trials,  
12 bringing products to market?

13 A. Yes. Our responsibility was  
14 in doing the clinical trials that led to  
15 the approval of a number of drugs, but  
16 most importantly at that time an  
17 anti-effective called ceftriaxone.

18 Q. And before you joined  
19 Janssen, did you work for another  
20 pharmaceutical company?

21 A. Yes. I worked for  
22 Rhone-Poulenc R-H-O-N-E, P-O-U-L-E-N-C,  
23 Rhone-Poulenc Pharmaceuticals in  
24 Princeton, New Jersey for approximately

1 five years.

2 Q. And what did you work on  
3 there?

4 A. The anti-infective area.  
5 We -- the primary area of research was  
6 early development of HIV compounds.

7 Q. And when did you move to  
8 Janssen?

9 A. In 1990.

10 Q. And your initial position  
11 there was what?

12 A. As the director of the  
13 anti-infective group within Janssen  
14 Research Foundation.

15 Q. And can you just give a  
16 capsule description of what you did at  
17 Janssen Research Foundation and for how  
18 long?

19 A. I was at Janssen Research  
20 Foundation for ten years. The Research  
21 Foundation was primarily responsible for  
22 the Phase II and III, the clinical trials  
23 that led to showing the effectiveness and  
24 safety and risks and efficacy of drugs

1     that we were looking to bring to the  
2     market.

3                     So it was a clinical  
4     development program. I was well versed  
5     in the issues and the regulatory issues  
6     around clinical trial methodology that  
7     would support the safety and efficacy and  
8     benefit-risk ratio of the products that  
9     we brought to market.

10            Q.     And when did you first  
11     become involved with the pain products  
12     that Janssen had?

13            A.     In the year 2000 when I  
14     moved over to the medical affairs group.

15            Q.     And what was your position  
16     there?

17            A.     Group director of the pain  
18     and mycology area, mycology being  
19     anti-fungals. I retained my  
20     responsibilities for some of the  
21     anti-infective compounds, but I was  
22     brought on primarily to develop a group  
23     that would be responsible for the pain  
24     products.

1           Q.     And some of those pain  
2     products were Schedule II opioid  
3     medications, correct?

4           A.     Correct.

5           Q.     Can you -- can you tell us  
6     which ones those were?

7           A.     That was Duragesic, the  
8     transdermal fentanyl patch.

9           Q.     And were there others later?

10          A.     Yes. And later that  
11     include -- well, it included other  
12     formulations of fentanyl that we were  
13     developing, that we -- that we provided  
14     input into development into the R&D  
15     program. But a drug that did come to  
16     market was Nucynta, N-U-C-Y-N-T-A, which  
17     is -- the generic name is tapentadol.

18          Q.     And you're now retired,  
19     right?

20          A.     Yes.

21          Q.     And when did you retire?

22          A.     In May of 2011.

23          Q.     So you've now come back as a  
24     consultant to help the company meet its

1 obligations to provide information in  
2 this litigation?

3 A. Yes.

4 Q. And is that a paid  
5 consulting job?

6 A. Yes, it is.

7 Q. So you're paid for your  
8 time. How are you paid?

9 A. I'm paid for my time.

10 Q. And at what rate?

11 A. At a rate of \$375 an hour.

12 Q. All right. Let's go back to  
13 your time in medical affairs at Janssen  
14 in the pain group starting in 2000. Just  
15 quickly, can you run through the general  
16 roles and -- role and responsibilities of  
17 that group in connection with Janssen's  
18 pain medicines?

19 A. The medical affairs group in  
20 general, in contradistinction to the R&D  
21 groups, was responsible for marketed  
22 products. So these are products that the  
23 FDA had already approved and which were  
24 marketed in the United States. And we

1 would have a cross-functional team, we  
2 were part of a cross-functional team that  
3 explored opportunities to provide  
4 additional data, postmarketing data, that  
5 would expand the body of knowledge around  
6 the specific drug.

7 The clinical trials that  
8 generally lead to approval of a product  
9 are somewhat limited and they meet the  
10 criteria that the FDA sets out for  
11 providing adequate data to assess  
12 efficacy and safety of a drug, but don't  
13 necessarily meet the information that  
14 the -- the healthcare community and  
15 treating physicians might need,  
16 information such as comparative data  
17 against other drugs. Information on  
18 subsets of patients, information on  
19 issues other than straightforward  
20 efficacy and safety. That might include  
21 specific adverse events or functionality,  
22 in the case of -- of pain medicines. And  
23 the medical affairs group led a  
24 cross-functional team that assisted in

1 developing some of those data.

2 Q. And how would your group go  
3 about developing data like that?

4 A. We would be involved early  
5 on in the early development of a compound  
6 in determining what data would be  
7 developed for the initial approval based  
8 upon the data that would be developed for  
9 the initial approval.

10 We might even at that point  
11 give input to endpoints that might be  
12 included in those trials, but generally  
13 without overcomplicating those trials.

14 But understanding what the  
15 additional needs of the healthcare  
16 community might be after the approval, we  
17 would, based upon those data, meet with  
18 healthcare providers, the treating  
19 community, experts in the field of, in  
20 this case, pain, to get their input to  
21 what additional data needs might be out  
22 there, what are the opportunities for us  
23 to develop those data streams and how  
24 best to do those things.

1                   It certainly goes beyond  
2     just the realm of clinical trials. We  
3     would look at all of the potential groups  
4     that might be using the drug. That --  
5     that would include pharmacy, pharmacy  
6     benefit managers, and the type of  
7     information that they might need to tier  
8     a product, to put the product on  
9     formulary. So a broad range of  
10    additional data that might prove useful  
11    after the drug receives its initial  
12    approval.

13                Q.     And did medical affairs  
14    participate in other cross-functional  
15    areas of -- of the pain drugs, for  
16    example, safety, communications,  
17    promotional review, can you describe  
18    those?

19                A.     Yes. As I said, there are a  
20    whole broad range of activities that  
21    medical affairs was involved with. We  
22    had representatives to a promotional  
23    review committee. There -- this is a  
24    committee that reviewed pieces that were

1 contemplated to be used as part of the  
2 promotion of the drug.

3 Medical affairs included not  
4 just the physicians within my group, but  
5 the medical information group, PharmDs  
6 who would assess the accuracy of the  
7 information that would be provided in  
8 promotional review. They would review  
9 the source documents that were being used  
10 to -- to provide the information that was  
11 in the -- the promotional materials.

12 We would have opportunities  
13 to do additional studies that even  
14 wouldn't be conducted under the auspices  
15 of the medical affairs group, so we would  
16 explore potential investigator-initiated  
17 studies where there was an interest in  
18 doing work with some of our compounds to  
19 expand the basis of knowledge, but didn't  
20 necessarily fall within the budgets or  
21 timelines that we might be able to fund  
22 internally, and we would consider funding  
23 those externally.

24 Q. What about safety reviews

1 and surveillance? Just generally, I'm  
2 going to come back to this.

3 A. When we had -- well, safety  
4 was an ongoing manner that -- that we  
5 followed our drugs. There was a safety  
6 group and all reports of adverse events,  
7 this is -- this is in addition to the  
8 adverse events that we learned of in the  
9 formal clinical trials that led to  
10 approval. There is a requirement  
11 subsequent to that that any additional  
12 clinical trials report, the safety to the  
13 safety group, reports that would come in  
14 from outside both patients and healthcare  
15 providers, and, in fact, anyone within  
16 the company who learned of an adverse  
17 event. I think I mentioned that even as  
18 a retiree, I have the responsibility for  
19 reporting adverse events that I learned  
20 about with -- with our compounds. And --  
21 and so we would meet with the safety  
22 group and assess those.

23 Where we had additional  
24 mechanisms in place to assess risks

1 associated with our compound, in the case  
2 of Duragesic, we had risk management  
3 plans that -- that followed databases and  
4 other means of getting information about  
5 risks of abuse, misuse, diversion, safety  
6 issues for fentanyl in general, other  
7 scheduled opioids, and Duragesic.

8 We would review those data  
9 streams and determine whether there were  
10 additional activities that -- that we  
11 needed to be taking. Those activities  
12 might be changes in package inserts,  
13 changes in educational material.

14 Q. All right. Well, before we  
15 come back to that, let's talk a little  
16 bit more about Duragesic. I think you  
17 said, Duragesic was already on the market  
18 when you started the pain group, medical  
19 affairs group. How long had it been on  
20 the market?

21 A. It was -- in the United  
22 States it was approved in 1990. So it  
23 had been on the market for ten years.

24 Q. And what is Duragesic?

1           A.       Duragesic is a reservoir  
2     patch, a form-filled and sealed reservoir  
3     patch, so the active ingredient is in a  
4     patch that is designed to deliver a  
5     controlled amount of fentanyl through the  
6     membrane and then through the skin; you  
7     apply the patch to the skin. And it  
8     releases fentanyl in a controlled manner  
9     over a period of approximately three  
10    days, 72 hours.

11           Q.       And what is fentanyl?

12           A.       Fentanyl is a potent opioid.  
13    The opioid class of drugs are drugs that  
14    attach to the -- certain receptors in the  
15    body, called mu opioid receptors. And  
16    these receptors are involved in  
17    modulation of pain.

18           Q.       And is fentanyl used in pain  
19    products besides Duragesic or other -- or  
20    other pain pills?

21                    Is it used in hospitals for  
22    example?

23           A.       Yes. Fentanyl is --  
24    fentanyl was originally synthesized I

1 believe around the 1960s and had been  
2 used as an anesthetic agent for decades.  
3 It was also commonly in use in -- as an  
4 intravenous administration for  
5 postoperative care where, in a hospital  
6 setting, along with other compounds, it  
7 might be used for patient-controlled  
8 anesthesia, so postoperatively a patient  
9 might have the ability to inject himself  
10 or herself with a controlled amount of  
11 intravenous fentanyl to control their  
12 postoperative pain.

13 Q. And how is fentanyl  
14 regulated?

15 A. Fentanyl is regulated under  
16 regulations of the drug -- Drug  
17 Enforcement Agency and the Food and Drug  
18 Administration. It's a scheduled  
19 product. It's -- it is a Schedule II  
20 product. Schedule II products are those  
21 products that are considered to have  
22 therapeutic values, but have the highest  
23 propensity for abuse, misuse and  
24 diversion, and so they are highly

1 regulated in terms of -- of distribution  
2 and the access to the drugs.

3 Q. And fentanyl is what's  
4 called the active ingredient in the  
5 Duragesic skin patch?

6 A. Yes.

7 Q. So it's -- but it's  
8 delivered through a patch, as opposed to  
9 through an IV or by an anesthesiologist?

10 A. That's correct. It goes  
11 through the membrane of the patch that's  
12 attached to the patient's skin, and then  
13 through the patient's skin into the  
14 bloodstream.

15 Q. Now, have you heard of  
16 illegally manufactured fentanyl or street  
17 fentanyl?

18 A. I have.

19 Q. And have you heard names,  
20 for example, that goes by?

21 A. Yes. It's widely known that  
22 fentanyl is an attractive drug of abuse  
23 and misuse and is sought after. Even in  
24 some of our own surveillance, we were

1 well aware that there were -- there were  
2 illicit laboratories, laboratories  
3 outside the United States that  
4 manufactured fentanyl or closely related  
5 compounds to fentanyl, and they would  
6 have a variety of street names, one of  
7 which we came to be -- which was familiar  
8 to us was China white.

9 Q. And is that the same thing  
10 as the fentanyl that's used in these  
11 hospital settings or in the Duragesic  
12 patch?

13 A. No, it's not.

14 Q. And how is it different?

15 A. Well, it's certainly not  
16 controlled in any sense of the controls  
17 that are in place for a pharmaceutical  
18 grade product where stringent guidelines  
19 around specifications for manufacture,  
20 the supply chain is carefully controlled.  
21 We know exactly what goes into the  
22 product, the concentration of the  
23 product.

24 We have no idea how an

1 illicitly manufactured product might be  
2 made or even if it's identical to the  
3 product fentanyl.

4 Q. And does that affect how  
5 dangerous the product is?

6 A. It certainly could, if -- in  
7 most instances where the product is  
8 obtained illicitly, the recipient might  
9 have, first of all, no idea whether the  
10 product he or she is using even contains  
11 fentanyl. There have certainly been  
12 reports of fentanyl-tainted heroin, where  
13 an individual expected that he or she was  
14 trying to use heroin but in fact was  
15 using fentanyl.

16 Even if they sought  
17 fentanyl, it would not be in a controlled  
18 dosage, the way a Duragesic patch is  
19 provided.

20 Q. Getting back to the  
21 Duragesic patch, which you said had been  
22 on the market for ten years when you  
23 became the pain director. What did you  
24 do to learn about that product when you

1       came into that position?

2                   A.       I familiarized myself with  
3       the package insert, with the clinical  
4       trials that were conducted to support the  
5       pharmacokinetics. I certainly learned  
6       about the pharmacokinetic profile and the  
7       ability of the patch to deliver a  
8       controlled rate of release over the three  
9       days. The clinical trials that led to  
10      approval, that led to -- led the FDA to  
11      assess the safety and efficacy of the  
12      product --

13                  Q.       Let's pause for a second on  
14      the package insert. Just broadly -- and  
15      we'll come back to it later. But what  
16      information does that provide, the  
17      package insert?

18                  A.       So in -- so a package insert  
19      is all of the important information that  
20      a prescriber would need to prescribe the  
21      product. That would include such things  
22      as the indications, what the product is  
23      indicated for; the selection of the dose  
24      for the patient; choosing the patient

1 properly; assessing the patient for the  
2 potential for adverse events; in the case  
3 of Duragesic, certainly, the information  
4 on how to monitor that patient over a  
5 period of time to assess that the patient  
6 continues to get the benefits of the  
7 product with reasonable tolerability;  
8 education that the healthcare provider is  
9 to share with the patient so that he or  
10 she uses the product appropriately and  
11 does not misuse it in ways that they  
12 might accidentally do so.

13 Q. And the --

14 A. Those are the key elements  
15 that we are providing to the physician.

16 Q. The package insert would  
17 describe, for example, how the product  
18 works chemically, how it's absorbed in  
19 the body, those kinds of things as well?

20 A. Yes. That would be part of  
21 the package insert.

22 Q. And what else did you do to  
23 familiarize yourself to learn about the  
24 product?

1           A.       In a general sense, I  
2       familiarized myself with some of the key  
3       concepts around pain management,  
4       particularly pain management with  
5       opioids; the issues of abuse, misuse and  
6       diversion; the other opioids that were  
7       available; differences between immediate  
8       release and controlled-release opioids;  
9       other compounds that are used to treat  
10      pain; the process of scheduling.

11                   Familiarized myself with  
12      some of the experts in the field and some  
13      of the work that was continuing around  
14      issues of effectiveness, abuse, misuse,  
15      diversion. In a broad sense becoming  
16      familiar with the -- with the entire  
17      range of pain management.

18           Q.       And did you have others  
19      working with you in this role?

20           A.       I did.

21           Q.       And who were they?

22           A.       Well, specifically one of  
23      the earliest activities that I embarked  
24      on was to bring the ENA physician who had

1 specific training. This was an  
2 individual trained as an  
3 anesthesiologist, and anesthesiologists  
4 are experts at using controlled  
5 substances.

6 We spoke already about the  
7 use of fentanyl as an anesthetic agent.  
8 And so I brought somebody in who had  
9 expertise in pain management issues and  
10 clinical trial methodology.

11 Q. And did you have access to  
12 others at Janssen who had medical  
13 expertise in these areas?

14 A. Yes. I think I indicated  
15 that medical affairs was a  
16 cross-functional group. We interacted  
17 certainly with the research and  
18 development side, where there were a  
19 number of physicians who had expertise in  
20 pain management and clinical trial  
21 development.

22 We interacted with the  
23 outcomes research group, and they had  
24 individuals who had expertise as well. I

1 had access to the manufacturer of the  
2 product, individuals at ALZA who also had  
3 some of the history of the development of  
4 the product.

5 Q. So let's talk a little bit  
6 about the benefits and risks of  
7 Duragesic. But before we start that, can  
8 you explain which patients the medication  
9 is intended for?

10 A. Yes. If you go to the  
11 indications, even early on, this was  
12 indicated for patients with moderate to  
13 severe chronic pain, individuals who  
14 would benefit from treatment with a  
15 long-acting opioid after proper patient  
16 selection, individuals who generally had  
17 been -- were tolerant of other opioids,  
18 had received other opioids, for whom  
19 other treatment options either didn't  
20 work or could not be used perhaps because  
21 they had contraindications to other  
22 medications or they had had adverse  
23 events for the other medications.

24 Q. So can you give some

1 examples of other treatment options?

2 A. Sure. Patients with pain  
3 might be treated with -- well non --  
4 non-pharmaceutical interventions. They  
5 might be treated with cognitive  
6 behavioral therapy; physical therapy  
7 initially; with milder analgesics that  
8 would include acetaminophen, nonsteroidal  
9 anti-inflammatories, such as ibuprofen,  
10 or naproxen.

11 There were also milder  
12 opioid options out there, and opioids  
13 with short duration of action.

14 Q. And to find the indication  
15 for the product, where would we find  
16 that, what you just described?

17 A. It's under the indications  
18 section of the package insert.

19 Q. Let's just get one out.

20 MR. LIFLAND: Do we have the  
21 2005 label?

22 MR. RODRIGUEZ: Do you have  
23 that in your package?

24 MS. CONROY: That, we do.

1 MR. LIFLAND: Let's hand it  
2 out, and -- otherwise we're --

3 MS. CONROY: I have no  
4 question we have it. It's in the  
5 packet -- it's in about eight  
6 boxes that you gave to us  
7 yesterday. So thank you. We only  
8 need one.

9 (Document marked for  
10 identification as Exhibit  
11 Janssen-Moskovitz-32.)

12 BY MR. LIFLAND:

13 Q. I'm marking this document as  
14 Exhibit 32. It begins with  
15 JAN-MS-00780844. It ends with  
16 JAN-MS-00780887.

17 A. Thank you.

18 Q. Dr. Moskovitz, can you tell  
19 me what this document is?

20 A. This is what is commonly  
21 referred to as the package insert.  
22 Technically it's the full prescribing  
23 information for Duragesic.

24 Q. And these package inserts

1 are regulated by the FDA, correct?

2 A. Yes, they are.

3 Q. And do they change over  
4 time?

5 A. They do.

6 Q. So you would need to look to  
7 see when this package insert was in  
8 effect, if we wanted to know what period  
9 of time it applied to?

10 A. Yes.

11 Q. Take a look at -- you may be  
12 able to tell just by glancing at it which  
13 period of time, but if you go to --

14 A. The date would usually be on  
15 the last page.

16 Q. Well, let me -- let me just  
17 represent to you that this is the 2005  
18 package insert, you might be able to look  
19 at it, look at the contraindications and  
20 just -- oh, I'm sorry, yes. The last  
21 page here, the very last page of the  
22 document.

23 A. Okay. The very last page of  
24 the document I have is -- oh, of the

1 document.

2 Q. No, no, the last page with  
3 the signature at the last page. Is there  
4 a date there?

5 A. There is. 2/4/05.

6 Q. So that's 2005?

7 A. Yes.

8 Q. Okay. Now, can you turn to  
9 where a doctor would find the indications  
10 for the product?

11 A. So in the black box you'll  
12 see, "Duragesic is indicated for  
13 management of persistent moderate to  
14 severe chronic pain that requires  
15 continuous around-the-clock opioid  
16 administration for an extended period of  
17 time and cannot be managed by other means  
18 such as nonsteroidal analgesics, opioid  
19 combination products, or immediate  
20 release opioids."

21 Q. So that's what you were  
22 talking about in terms of what products  
23 the -- the product -- or what patients  
24 the product is intended for?

1           A.       That's correct. The -- the  
2       patients who have this indication would  
3       be considered for -- might be considered  
4       candidates for Duragesic.

5                   Then on -- the specific  
6       indications of usage is really a repeat  
7       of what I just gave you that was in the  
8       black box. And that's on JAN-MS-0780852.

9                   I don't have to repeat it.  
10      It's the same indication.

11           Q.       And are you aware of whether  
12      this indication from 2005 has changed  
13      since then?

14           A.       Yes, it has. I believe the  
15      current indications are similar, but the  
16      wording indicates that it's for  
17      management of pain that's severe enough  
18      to require around-the-clock treatment.

19                   I'd have to go back to the  
20      exact wording. But it does change over  
21      time as more information becomes a  
22      available and the benefits/risks are  
23      assessed.

24           Q.       But it's still for patients

1     who require continuous around-the-clock  
2     opioid administration for an extended  
3     period of time?

4             A.     Yes. And patients with  
5     chronic pain -- again, this is moderate  
6     to severe. Ultimately recurrent is for  
7     severe enough.

8             Q.     Can it be used for acute  
9     pain?

10            A.     It should not be used for  
11    acute pain.

12            Q.     And it is -- is that  
13    indicated somewhere in the package  
14    insert?

15            A.     If you -- even within the  
16    black box, the second bullet, it  
17    should -- it's contraindicated, which is  
18    to say it should not be used, "In the  
19    management of acute pain or patients who  
20    require opioid analgesic for a short  
21    period of time."

22            Q.     And has the -- does the  
23    indication limit the kinds of chronic  
24    pain for which the product may be used?

1           A.       No, it's indicated for  
2 chronic pain.

3           Q.       Has that always been the  
4 case?

5           A.       Yes, it has.

6           Q.       So it wouldn't be limited  
7 for example, to chronic pain from cancer?

8           A.       That's correct.

9           Q.       It could be any kind of  
10 chronic pain?

11          A.       Chronic pain that meets the  
12 criteria of persistent around-the-clock  
13 need for an analgesic, yes.

14          Q.       Back to the question about  
15 the benefits and risks. What are the  
16 benefits of the Duragesic patch for the  
17 patient?

18          A.       So to begin with, fentanyl  
19 itself is a potent opioid that attaches  
20 to the mu opioid receptor. It's a  
21 well-known receptor that modulates pain.

22                   We developed Duragesic such  
23 that it delivers fentanyl in a controlled  
24 manner so that the drug is delivered

1 transdermally over a period of 72 hours,  
2 approximately three days.

3 Q. What's the importance of  
4 having a controlled dose?

5 A. Well, so to begin with it  
6 allows you to have less frequent dosing.  
7 But also a controlled dose minimizes, in  
8 pharmacokinetic terms, peaks and trough.  
9 So you have lower high concentrations as  
10 the drug is coming into the bloodstream,  
11 and you don't go as low as -- as an  
12 orally administered drug as the drug  
13 wears off. And that is thought to  
14 minimize the potential for abuse and  
15 addiction. It allows the patient to  
16 potentially not focus on their pain for  
17 the extended period of time. We are  
18 aware of concerns from physicians that  
19 patients were focused on when they could  
20 take their next pill, and -- and this  
21 allows for a period of -- of three days  
22 with continuous pain relief that  
23 potentially would allow the patient to  
24 get back to their activities of daily

1     living.

2             Q.     Is there still a potential  
3     for abuse with the patch?

4             A.     Absolutely. Fentanyl is  
5     recognized as a Schedule II drug with  
6     a -- a high risk of abuse and misuse --  
7     abuse, misuse and diversion.

8             Q.     Is that a topic that's  
9     similarly addressed in the package insert  
10    as well?

11            A.     It is. Actually right from  
12    the -- in the very first paragraph,  
13    "Schedule II opioid substances which  
14    include fentanyl have the highest  
15    potential for abuse and associated risk  
16    of fatal overdose due to respiratory  
17    depression. Fentanyl can be abused and  
18    is subject to criminal diversion."

19            Q.     Can you just explain quickly  
20    what that -- what is meant by "overdose  
21    due to respiratory depression"?

22            A.     So the most serious adverse  
23    events of too high a concentration of  
24    opioids, they suppress respiration. So

1     you will -- with a high enough  
2     concentration, the patient will stop  
3     breathing. And if that isn't reversed  
4     rather quickly the patient could sustain  
5     brain injury or death.

6             Q.     And I take it that's the  
7     principle reason why it's so important to  
8     have a controlled and predictable dose in  
9     the delivery system?

10            A.     Yes.

11            Q.     Now, is there more  
12     discussion in the package insert around  
13     these issues of potential abuse and  
14     potential overdose?

15            A.     Yes. Throughout the package  
16     insert these issues are reiterated. What  
17     I've read to you for the most part is in  
18     the black box. So this is highlighted  
19     for the treating physician, but similar  
20     concepts are presented throughout the  
21     package insert.

22            Q.     For example in the -- take a  
23     look at Page 10. There's a section  
24     titled Contraindications.

1 A. Yes.

2 Q. Can you explain what that  
3 is?

4 A. So contraindications is an  
5 absolute, do not give the drug to  
6 patients who meet any of these criteria.

7 Q. And the first one is in  
8 patients who are not opioid tolerant.  
9 Can you explain that?

10 A. Yes. So the concept of  
11 tolerance is that patients who have  
12 already been exposed to doses of opioids  
13 that would equate with a dose of  
14 fentanyl. If you -- that you shouldn't  
15 be using fentanyl as the first opioid in  
16 an individual. The individual should  
17 have been exposed to other opioids before  
18 beginning treatment with fentanyl.

19 Q. And what's the reason for  
20 that?

21 A. Because there is a risk of  
22 the patient developing respiratory  
23 depression even with the first dose of  
24 fentanyl if they are not opioid tolerant.

1           Q.       Okay. The second one you  
2 spoke about earlier is acute pain. And  
3 then there's a reference for management  
4 of postoperative -- postoperative pain.  
5 Do you know the reason for that  
6 contraindication?

7           A.       We were aware that there  
8 were instances of misuse of the product  
9 in treating patients with postoperative  
10 pain which would fall under the -- the  
11 general category of acute pain. And  
12 there were adverse events and deaths  
13 associated with the use of the Duragesic  
14 patch in treating some of these  
15 individuals with postoperative pain.

16          Q.       And then the next two, we  
17 have mild pain and intermittent pain.  
18 Can you explain those?

19          A.       Yes. So even if you go back  
20 to the original studies, the original  
21 studies enrolled patients with moderate  
22 to severe pain. Mild pain can be managed  
23 with modalities other than a Schedule II  
24 long-acting opioid. So, therefore, you

1     should be using other compounds to treat  
2     mild pain.

3                     Intermittent pain is not  
4     pain that's around-the-clock that can be  
5     generally managed with intermittent  
6     dosing of other compounds or short-acting  
7     opioids.

8             Q.     Now, if you'll turn to the  
9     next page you'll see there's a section  
10    entitled "Misuse, Abuse and Diversion of  
11    Opioids." And this is addressed to the  
12    risks that you pointed out previously in  
13    the black box warning; is that correct?

14            A.     Yes.

15            Q.     But gives a more thorough  
16    discussion?

17            A.     Yes.

18            Q.     And then the next section on  
19    the next page, hypoventilation, that's  
20    another word for respiratory depression?

21            A.     Yes.

22            Q.     So that's the risks of  
23    overdosing and essentially having your  
24    breathing stopped if you don't --

1           A.       If you don't reverse it  
2       quickly.

3           Q.       Now, I'm not going to go  
4       through the whole thing, but I would like  
5       you to turn to Page 17. And this is a  
6       reference to drug interactions. Can you  
7       explain what that is?

8           A.       So a physician should take a  
9       careful history of other medications that  
10      a patient is on because, as with a lot of  
11      medications, concomitant medications may  
12      interact with the compound that you're  
13      prescribing, in this case with fentanyl.

14                   An example of that, there  
15      are other drugs that might be metabolized  
16      through the same system that metabolizes  
17      fentanyl to inactive compounds. If  
18      you're taking such drugs, that may slow  
19      the metabolism of Duragesic and lead to  
20      concentrations that are higher than would  
21      be predicted if you didn't take those  
22      concomitant medications.

23                   There are other medications  
24      that contribute physiologically to the

1 effects of opioids that might lead to  
2 increased sedation or decreased  
3 respiratory drive.

4 Q. If you turn to Page 23, do  
5 you see there's a section entitled "Drug  
6 Abuse and Addiction"?

7 A. Yes.

8 Q. And if you turn to Page 24,  
9 another section entitled "Overdosage."

10 A. Yes.

11 Q. So this is giving the  
12 physician even more information on those  
13 risks, correct?

14 A. Correct.

15 Q. And then under that it's  
16 "Dosage and Administration." Can you  
17 explain what that section is intended to  
18 convey?

19 A. Yes. So this is intended to  
20 instruct the healthcare provider, the  
21 prescriber, in general principles of  
22 prescribing opioid narcotics, especially  
23 Schedule II narcotics, but also in giving  
24 direction to how to select the dose of

1 Duragesic and how to monitor and change  
2 that dose as needed.

3 Q. All right. Now, let's go  
4 back to Page 15. You'll see there's a  
5 section entitled "Information For  
6 Patients." What's the purpose of this  
7 section?

8 A. The physician -- the  
9 healthcare provider, the prescriber, is  
10 instructed on information that he or she  
11 should be providing to the patient to  
12 ensure that the drug is used safely and  
13 that it's -- to minimize any risk of  
14 diversion or access by someone other than  
15 the patient, how the patient is to store  
16 the drug and concerns about manners in  
17 which there might be an uncontrolled  
18 delivery or greater than expected  
19 delivery of fentanyl.

20 Q. And can you give some  
21 examples of that?

22 A. Yes. So there's  
23 instruction. If you look on Page 16  
24 under 4. The patient should be

1 instructed not to use the patch if the  
2 seal is broken, altered, cut in any way  
3 because that defeats the  
4 controlled-release of the product.

5 In Number 5, we ask that the  
6 patient be instructed not to -- to avoid  
7 exposure to heat sources because  
8 potentially heat sources could increase  
9 the flux of fentanyl. And again, the  
10 patient would receive a greater than  
11 expected dose of fentanyl.

12 They are instructed on how  
13 to dispose of the drug when they finish  
14 using it so as to minimize access by  
15 anyone other than the patient, and  
16 ultimately to fold the product and flush  
17 it down the toilet so that it isn't even  
18 available in a waste basket.

19 Q. And is this information  
20 given directly to the patient as well in  
21 written form?

22 A. Yes. We also developed a  
23 patient medication guide so that much of  
24 this information is provided directly to

1 the patient through the medication guide  
2 that the patient is to receive with each  
3 and every refill of the prescription.

4 Q. Take a look at -- I think  
5 the numbering re-starts. It's after the  
6 end of the document, which is Page 33.  
7 If you look at the page after that.

8 A. Yes, I have it.

9 Q. Can you tell us what that  
10 is?

11 A. This is a patient  
12 information. So this is to be provided  
13 to the patient. It's written in an  
14 easier to understand -- in fact, it has  
15 to reach -- it has to be written to  
16 certain guidelines of understanding so  
17 that it's easy for the patient to  
18 understand. And it provides much of the  
19 same information about the appropriate  
20 use of the product and the appropriate  
21 storage and the appropriate disposition  
22 of the product.

23 Q. And it also -- let's turn a  
24 few pages in, it gives the basic

1 instructions as to how to actually put  
2 the patch on the skin, for example.

3 A. That's correct.

4 Q. And this one is called  
5 patient information sheet. You referred  
6 to it as a patient information guide or  
7 medication guide?

8 A. Medication guide. That was  
9 the term that came to be used under the  
10 formal REMS program.

11 Q. Now, did you have  
12 information at the company about how easy  
13 or difficult the patch was to abuse for  
14 somebody who would try to use it for  
15 nonmedical purposes?

16 A. There are various sources  
17 where we learned of the methods that  
18 would be tried to abuse and misuse and  
19 divert the product.

20 Q. And what did you -- what did  
21 you generally learn? And we'll talk  
22 about first the reservoir patch, the one  
23 that was there when you came into the  
24 position.

1           A.       So among the -- or what we  
2       learned that it was not an attractive  
3       formulation for abuse, misuse and  
4       diversion. It was rather difficult to  
5       use through a variety of sources, not the  
6       least of which was internet monitoring.

7                       We understood that it was  
8       not a preferred route of delivery. Most  
9       addicts or individuals who sought the  
10      high from an opioid compound would seek a  
11      pill. It was difficult to get a known  
12      quantity of the drug. And in fact, we  
13      learned that -- word on the street that  
14      we saw in some of the monitoring was that  
15      it was too great a risk for serious  
16      adverse events and even death.

17           Q.       So even -- even addicts  
18      would be worried about the risks they  
19      were taking with trying to use this as a  
20      drug of abuse?

21                       MS. CONROY: Objection.

22                       THE WITNESS: That was one  
23      of the things that we came to  
24      understand in the monitoring

1 programs.

2 BY MR. LIFLAND:

3 Q. And can it be snorted like a  
4 pill?

5 A. You can attempt to.

6 Q. Is it easier or more  
7 difficult?

8 A. It's more difficult to --  
9 than you -- because you have fentanyl in  
10 an alcohol base and a gel base. It's  
11 difficult to snort or to smoke or to  
12 inject the compound.

13 Q. At some point in time, the  
14 company changed the way the patch was  
15 formulated and went from the gel-based  
16 patch that we've been talking about where  
17 the fentanyl is dissolved in an alcohol  
18 gel, to what's called a matrix design.  
19 Can you explain what that is?

20 A. Yes. A matrix design would  
21 almost be described as fentanyl in a  
22 solid formulation where the fentanyl is  
23 evenly distributed throughout the solid  
24 patch, not a liquid patch. You wouldn't

1     see liquid as you would if you opened  
2     a -- the original fentanyl reservoir  
3     patch. This would be a solid piece of  
4     patch.

5             Q.     When did the company first  
6     start looking at the matrix design for  
7     the patch?

8             A.     We looked at the matrix  
9     design, I believe, around 2000.

10            Q.     And I take it there would be  
11    some advantages to the matrix design  
12    would be a reason to look at it, can you  
13    describe what those would be?

14            A.     Yes. For one thing it  
15    couldn't -- it couldn't leak. So one of  
16    the concerns around Duragesic was if you  
17    cut the patch or if there were a problem  
18    with manufacturing, there could be  
19    leakage of the fentanyl. That would not  
20    happen with a matrix.

21            Q.     And you said you first --  
22    the company first looked at it in 2001.  
23    Did the company decide to go forward with  
24    the matrix patch in 2001?

1 A. Not in the United States.

2 Q. And why not?

3 A. We commissioned a -- a  
4 review of the potential for abuse,  
5 misuse, diversion with a matrix patch and  
6 the experts that did that review  
7 concluded that there were risks  
8 associated with the matrix patch that  
9 were not present with a reservoir patch  
10 and that those risks might lead to  
11 increased abuse, misuse and diversion.

12 Q. And were those risks that  
13 the company had actually seen in people  
14 using the matrix patch?

15 A. Yes, but to a fairly low  
16 degree.

17 Q. And this is in 2001?

18 A. This is in 2000, 2001 --  
19 well, it's -- it's throughout the history  
20 of -- from 2000 on -- from 1999 on just  
21 based on adverse event reporting and  
22 clinical trials.

23 Q. And over the years did the  
24 company look further at the question of

1 the matrix patch as a possible  
2 alternative formulation?

3 A. Yes. In the United States  
4 we again commissioned, if you will, an  
5 update to the 2001 report because we were  
6 aware that there was potential for a  
7 matrix patch to be marketed in the United  
8 States and we asked whether the  
9 conditions or the -- the knowledge base  
10 we had in 2001 was still relevant.

11 Q. Now, when you commissioned  
12 these reports, did the reports give you  
13 information about what was happening in  
14 the real world with abuse of the patch  
15 that you had, the reservoir patch?

16 MS. CONROY: Objection.

17 THE WITNESS: Yes, that  
18 was -- yes, that was part of the  
19 report. So the reports went back  
20 and looked at databases that would  
21 inform about the relative risks of  
22 abuse, misuse and diversion.

23 BY MR. LIFLAND:

24 Q. And what information did

1       they give you on that subject?

2               A.       That through both periods of  
3       time, 2001 up to 2004, the Duragesic was  
4       not attractive as a drug of abuse, misuse  
5       and diversion. And that the rates, at  
6       least using the databases available at  
7       that time, remained consistently lower  
8       than other extended-release opioids.

9               Q.       Now, at a certain point in  
10      time the company did change the design  
11      and introduce the matrix patch in place  
12      of the reservoir patch; is that correct?

13              A.       That's correct.

14              Q.       Do you recall when that  
15      happened?

16              A.       Well, the -- the drug was  
17      approved for marketing in 2009.

18              Q.       And did the company, before  
19      doing that, did the company look again at  
20      the issues around the potential  
21      abusability of the matrix formulation as  
22      compared to the reservoir formulation?

23              A.       Yes, we did. So at that  
24      point, as I indicated, there was a matrix

1 patch that had been marketed in the  
2 United States since 2005. Certainly at  
3 that time there were other matrix patches  
4 that were on the market, but the first  
5 matrix patch was marketed in 2005. And  
6 so we had several years of data at that  
7 point in the 2008-2009 period to assess  
8 relative rates of abuse, misuse and  
9 diversion.

10 (Document marked for  
11 identification as Exhibit  
12 Janssen-Moskovitz-33.)

13 BY MR. LIFLAND:

14 Q. So I'm going to mark as  
15 Exhibit 33, it's JAN-MS-02578637 through  
16 38.

17 MS. CONROY: Thank you.

18 BY MR. LIFLAND:

19 Q. A memorandum. It's entitled  
20 Review and Conclusion of the RADARS  
21 Report Summarizing Abuse and Diversion  
22 Data For Transdermal Fentanyl Products in  
23 the United States. And it's signed on  
24 the second page by you, Bruce Moskovitz,

1 M.D.

2 A. Thank you.

3 Q. Can you explain what this  
4 document is?

5 A. Give me a moment to look at  
6 it.

7 Yeah, so this -- this  
8 summarizes the conclusion of the  
9 surveillance programs that we had in  
10 place, certainly before 2005, but we were  
11 looking at a comparison of the rates of  
12 abuse, misuse and diversion that might  
13 have occurred from the time that a matrix  
14 patch was available from 2005 on. And we  
15 looked at those rates through the various  
16 tracking systems that were subsumed under  
17 the, what was called RADARS, a number of  
18 different streams of data. And we  
19 concluded that through this period of  
20 time, approximately two to three years,  
21 the abuse and diversion of fentanyl  
22 patches remained low relative to other  
23 opioids. And that there was no  
24 compelling evidence to suggest that the

1 matrix formulation was abused or diverted  
2 more than the reservoir formulations.

3 At that time we concluded  
4 that we could safely move from a  
5 reservoir patch to a matrix patch in  
6 conformance with what the FDA preferred  
7 as the formulation.

8 Q. Let me shift the focus a  
9 little here. And again, let's talk about  
10 the issue of actions the company may have  
11 taken to encourage safe and effective use  
12 of the product and deter abuse and misuse  
13 of the patch. And now I'm talking about  
14 things beyond simply discussing the  
15 design of the patch and how that might be  
16 harder or easier to abuse.

17 Can you -- can you describe  
18 for me those, please?

19 A. Well, we --

20 Q. And you might want to start  
21 with the package insert.

22 A. Okay. So the package insert  
23 summarizes all of the pertinent  
24 information that a prescriber needs to

1 appropriately select the patient. Get  
2 the medical history that would inform the  
3 treating physician. Whether there were  
4 any contraindications or concomitant  
5 medications that -- that he or she should  
6 be aware of. Select the appropriate dose  
7 based upon the opioids that the patient  
8 had previously been exposed to. How to  
9 monitor that patient -- well, how to  
10 inform the patient, first of all, at the  
11 time that you're prescribing the drug,  
12 about the appropriate use of the product,  
13 the appropriate precautions that the  
14 patient should be taking. Things that  
15 we've already spoken about, such as not  
16 exposing the patch to heat sources. How  
17 to properly dispose of the patch. And  
18 the type of monitoring that the physician  
19 might be doing with the patient.

20 So we also instructed the  
21 physician about how to monitor the  
22 patient over the course of his or her  
23 therapy to continue to assess that the  
24 benefits that the patient would be

1 getting from Duragesic would continue to  
2 outweigh the risks of the -- the product.

3 Q. Okay. Well, let's -- let's  
4 break that down a little bit.

5 A. Okay.

6 Q. We looked at the -- at the  
7 package insert initially. And the  
8 initial thing we looked at was the  
9 descriptions of the risks.

10 So those are described here?

11 A. Yes.

12 Q. And then you mentioned  
13 patient selection, proper patient  
14 selection?

15 A. Correct.

16 Q. You mentioned proper dosing?

17 A. Correct.

18 Q. And you mentioned patient  
19 counseling?

20 A. Correct.

21 Q. And you mentioned proper  
22 monitoring?

23 A. Correct.

24 Q. So let's talk a little bit

1     about each of those.

2                     Patient selection, I gather  
3     initially that's looking at the --  
4     whether the patient fits the indication,  
5     at least that's one aspect of it?

6                     A.     Whether the patient fits the  
7     indication and the patient doesn't have  
8     any of the contraindications or any other  
9     concerns, even though they may not be  
10    contraindications, other drugs that the  
11    patient may be taking that might alter  
12    their -- their mental state or that might  
13    increase certain risks for some of the  
14    adverse events. So it's not just those  
15    that are contraindications.

16                    Q.     And proper dosing?

17                    A.     Yes.

18                    Q.     And that, I take it, is to  
19    ensure that the dose is -- to ensure that  
20    the dose is high enough for pain relief,  
21    but not so high that it places the  
22    patient in danger of hypoventilation?

23                    A.     I would start off by saying  
24    that the dose is low enough --

1 Q. Low enough.

2 A. -- to begin with, so that  
3 you begin from a place where you are not  
4 putting the patient at risk. And if  
5 higher doses are needed to achieve  
6 analgesia, you have an opportunity to  
7 increase those doses.

8 To -- there are tables in  
9 here and aids to assist the patient in  
10 choosing the proper dose of Duragesic  
11 based upon the opioid that the patient  
12 might be taking at the time he or she is  
13 transferred to Duragesic.

14 Q. And you mean to assist -- I  
15 assume you meant to say assist the doctor  
16 in choosing?

17 A. Yes. Assist the doctor in  
18 choosing the right dose based upon what  
19 the patient is taking at the time.

20 Q. And that process of starting  
21 at a lower dose and moving to the minimum  
22 that's needed, what is that called?

23 A. Well, titration of the  
24 patient.

1 Q. And then patient counseling.  
2 This is what you spoke about before in  
3 terms of giving the patient the  
4 information that they would need to  
5 minimize the risk of -- of adverse  
6 events?

7 A. Yes, and counseling the  
8 patient so that the patient is aware that  
9 he or she shouldn't be treated with the  
10 drug if the treatment is for acute pain  
11 or for pain that's not continuous,  
12 around-the-clock, persistent pain.

13 Q. And proper monitoring,  
14 what's the importance of proper  
15 monitoring?

16 A. Well, in a -- in a broad  
17 sense, the concept of patient management,  
18 especially with potent opioids, we would  
19 look at four aspects of treatment.  
20 Analgesia, how well are you achieving the  
21 goal of pain reduction. I mean you're  
22 treating the patient with an analgesic.  
23 You want to reduce their pain.

24 Adverse events, how well is

1 the patient tolerating the drug. Are  
2 they experiencing -- and we expect that  
3 many of the patients, particularly early  
4 in the course of therapy, may have some  
5 adverse events that may be tolerated or  
6 may diminish over time. Commonly for  
7 opioids, those might be constipation,  
8 gastrointestinal adverse events, itching,  
9 pruritis.

10 Okay. So we spoke about  
11 analgesia and adverse events.

12 Activities of daily living,  
13 one of the things that we like to achieve  
14 with pain medication is not just a  
15 reduction in pain but getting the patient  
16 back to those activities that might be  
17 important to him or her. And that has to  
18 be individualized to the patient, but  
19 it's a discussion that physicians should  
20 have. What does the patient want to do  
21 if we can relieve their pain?

22 And then elements that would  
23 help you determine whether there are  
24 behaviors associated with abuse and

1 misuse and assess those as well.

2 Q. Now, did you have data at  
3 Janssen that looked at the efficacy of  
4 the products, if it -- if it was used  
5 chronically, that is, over a longer term  
6 course of therapy?

7 A. Yes.

8 Q. And can you describe what  
9 those were?

10 A. So even going back to the  
11 original studies, and I'd have to  
12 refer -- the efficacy assessment was made  
13 over a period of 30 days. But some of  
14 those patients were treated for extended  
15 periods of time where they continued to  
16 gain the benefits of pain management.  
17 There are other studies that were  
18 subsequently conducted.

19 And in a number of those  
20 studies, the treatment period extended to  
21 a year or more. So we had a body of data  
22 that there were patients who would  
23 continue to benefit from continued use of  
24 Duragesic, where they would have pain

1 relief and have tolerable side effects  
2 over a long period of time.

3 Q. And because you have that  
4 data, does that mean that a doctor can  
5 simply place a patient on the medication  
6 for a long period of time and, you know,  
7 and set and forget?

8 A. No, of course not. The  
9 risks associated with opioids are  
10 substantial. And, therefore, a physician  
11 has to monitor the patient on a regular  
12 basis, monitor the patient for analgesia,  
13 adverse events, activities of daily  
14 living, and aberrant drug behaviors.

15 By virtue of it being a  
16 Schedule II, you can't even call in the  
17 prescription. You have to see the  
18 patient on a regular basis. So we are  
19 talking about a continual assessment  
20 of -- that the benefits of the medication  
21 continue to outweigh the risks associated  
22 with opioid therapy.

23 Q. For the particular patient?

24 A. For that particular patient,

1       yes.

2                   Q.       And you mentioned quality of  
3       life. Did the company have data on  
4       quality of life from improvements from  
5       opioid therapy with Duragesic?

6                   A.       Yes, there were a number of  
7       studies that included measures of quality  
8       of life. There are a number of surveys,  
9       there are a number of questionnaires and  
10      assessments that the clinician or the  
11      investigator can administer that assess  
12      functionality and quality of life. And  
13      we included those in a number of our  
14      investigations.

15                  Q.       And what is the importance  
16      of monitoring -- I think the last thing  
17      you said was signs of aberrant behavior.

18                  A.       As with other potent  
19      opioids, these are drugs that are used --  
20      abused, misused, diverted. So if a  
21      patient was exhibiting aberrant  
22      behaviors, early refills, I lost the  
23      drug, there are a variety of known  
24      behaviors that are classified as aberrant

1 drug behaviors that might suggest to the  
2 treating physician that he or she  
3 carefully determined whether continued  
4 use of the product is warranted. In some  
5 cases it may very well be. But you may  
6 need to put in place a more stringent  
7 monitoring avenues.

8 In some cases based upon  
9 those aberrant behaviors, you may choose  
10 to decrease the dose or even stop the  
11 dose or to refer the patient to a pain  
12 specialist who has more experience in  
13 managing a patient who might exhibit  
14 these aberrant behaviors.

15 Q. Are different patients at  
16 different risk for these kinds of adverse  
17 events?

18 A. Yes. We saw that in  
19 multiple publications over the course of  
20 time. You can almost construct a  
21 hierarchy where an older patient who does  
22 not smoke, does not have history of  
23 alcohol abuse or abuse of other drugs,  
24 would have among the lowest likelihood of

1 abuse, misuse and diversion, all the way  
2 to an individual who has pain that needs  
3 to be treated, but that individual has a  
4 history of substance abuse, alcoholism,  
5 other drugs of -- with euphoric  
6 capabilities, smoking, depression. There  
7 are a number of high risk conditions that  
8 would inform the treating physician that  
9 this is a patient who is at greater risk  
10 for issues of abuse, misuse and  
11 diversion.

12 Q. And what would that counsel  
13 in terms of patient monitoring?

14 A. That, again, would be  
15 individualized. So you would have to  
16 make a very careful assessment of the  
17 patient, of the starting dose. You might  
18 have a written agreement with the patient  
19 such that the patient would agree to have  
20 pill counts. The patient might agree to  
21 have urine testing on a regular basis.

22 Again, going back to the  
23 very outset, you might choose to refer  
24 that patient to a pain specialist to have

1     that individual who has much more  
2     expertise in treating high risk  
3     individuals, treat that patient, rather  
4     than primary care, if that's the -- what  
5     we're talking about. But -- or you might  
6     see the patient more frequently to assess  
7     whether that patient continues to gain  
8     the benefits of the drug and the  
9     benefit-risk ratio remains.

10           Q.     We've already looked, I  
11     think, at the information on these topics  
12     that's provided in the package insert.

13                     Were there other vehicles  
14     that the company used to provide this  
15     kind of information to physicians?

16           A.     Yes. We supported  
17     educational programs that taught about  
18     appropriate prescribing, appropriate  
19     monitoring. We supported websites that  
20     spoke about how to manage patients with  
21     pain. We developed tools that a  
22     physician could use to assess these  
23     aspects of pain management and document  
24     the interaction with the patient.

1 Q. Let me show you a document.  
2 It may take just a minute to find it  
3 here.

4 (Document marked for  
5 identification as Exhibit  
6 Janssen-Moskovitz-34.)

7 BY MR. LIFLAND:

8 Q. We marked this as  
9 Exhibit 34.

10 MS. CONROY: You are going  
11 to need it, right?

12 MR. LIFLAND: I think we  
13 have a third one.

14 MS. CONROY: You have --  
15 okay, great. Thank you.

16 MR. LIFLAND: And I'll put  
17 it up on the screen.

18 BY MR. LIFLAND:

19 Q. Can you tell me what this  
20 document is, Dr. Moskovitz?

21 A. Yes. This is a report on a  
22 tool that was developed in part with  
23 the -- the work that was done internally  
24 at Janssen to assess in relatively brief

1 and straightforward way those elements  
2 that we just spoke of. Steve Passik, who  
3 is the lead author, had developed the  
4 concept of -- of monitoring for the four  
5 A's: Analgesia, pain relief, adverse  
6 events, how well the patient tolerated  
7 the drug, activities of daily living, and  
8 aberrant drug use.

9 And this was a tool that was  
10 developed to help a physician assess  
11 those four areas of treatment and  
12 document them in a -- in a note with each  
13 patient visit.

14 Q. And is Janssen or a Janssen  
15 employee one of the authors on this?

16 A. Actually two, there are two  
17 Janssen employees, Sheri Dodd and Jeffrey  
18 Schein.

19 Q. And was this a tool that was  
20 provided to physicians so that they could  
21 use it for the patient monitoring that's  
22 recommended?

23 A. Yes, we -- we did provide  
24 it. Ultimately we had tear-off sheets so

1     that it could be provided to prescribers  
2     as a -- as a tool to use in documenting  
3     the four A's of patient management with  
4     an opioid.

5                     (Document marked for  
6                     identification as Exhibit  
7                     Janssen-Moskovitz-35.)

8     BY MR. LIFLAND:

9             Q.     And let me hand you another  
10     document. This will be Exhibit 35. And  
11     this is from the website of NIDA. And  
12     you -- do you know what NIDA is?

13            A.     National Institute on Drug  
14     Addiction.

15            Q.     And do you know what NIDA's  
16     mission is?

17            A.     Yes. They're -- they're --  
18     I couldn't give you it to you in exact  
19     unless I went to the website. But they  
20     want to develop scientific data that  
21     informs the scientific community, the  
22     treating community on issues related to  
23     public health abuse, misuse and issues of  
24     addiction. Scientifically based data

1       that do that.

2                   Q.       And -- and they have posted  
3       the PADT developed by Janssen as a tool  
4       on their website?

5                   A.       Yes. I don't know if we  
6       officially used the term "PADT." So the  
7       tool that we were speaking about that  
8       assessed these four A's of treatment was  
9       called the Pain Assessment and  
10      Documentation Tool and was shortened to  
11      the PADT.

12                  Q.       And take -- take a look at  
13      the second page. That's what it's  
14      referred to at the top there?

15                  A.       That's correct.

16                  Q.       And let me just ask you, is  
17      this a validated tool? Can you explain  
18      what that is, or is it just -- something  
19      short of that?

20                  A.       It -- it was -- it was not  
21      validated in the sense that it could  
22      actually predict whether by using the  
23      tool you could predict for issues of  
24      abuse, misuse and -- and diversion. But

1     it was understood that one of the -- one  
2     of the requirements for appropriate  
3     patient care, particularly if you're  
4     prescribing a scheduled product, is to  
5     continue to document in your notes the  
6     reasoning behind your decision to start a  
7     patient on drug or your decision to make  
8     any changes during the course of therapy  
9     or to continue therapy. And this was a  
10    tool that was developed to assist with  
11    that.

12               Q.     Let me turn now to the  
13    subject of safety surveillance. Were you  
14    involved with safety surveillance of the  
15    Duragesic and other pain products at  
16    Janssen?

17               A.     Yes.

18               Q.     And how did the company go  
19    about doing that?

20               A.     Well, safety surveillance  
21    goes all the way back to designing a  
22    clinical trial that would assess benefits  
23    and risks in the clinical trials, adverse  
24    events. The -- after the drug is

1 marketed there is a regulatory  
2 responsibility to report to the Food and  
3 Drug Administration on a periodic basis,  
4 more frequently initially, less  
5 frequently later on, adverse events and  
6 events of particular interest.

7 In the case of opioids, the  
8 events of particular interest might be  
9 such things as a respiratory depression,  
10 exposure, pediatric exposures, opioid  
11 naive exposures.

12 But we also put in place  
13 other mechanisms for monitoring, for  
14 abuse, misuse and diversion, monitoring  
15 databases such as DAWN, TESS databases,  
16 of forensic laboratory databases,  
17 internet databases.

18 Q. Let me -- let me --

19 A. Sure.

20 Q. Let me see if I can give you  
21 a document that will allow us to go  
22 through that a little bit more  
23 systematically.

24 I'm going to -- I'm

1 referring to Exhibit 28. It should be in  
2 your stack. It was marked earlier today.

3 A. I wish I was as good as you  
4 were about putting things in the --

5 MS. CONROY: I have one, I  
6 think, that does not have any  
7 writing on it, except for my  
8 Ex-28.

9 THE WITNESS: I think I have  
10 it here. Thank you.

11 MS. CONROY: Okay.

12 BY MR. LIFLAND:

13 Q. Dr. Moskovitz, do you  
14 recognize this document?

15 A. I do.

16 Q. And you -- you referred to a  
17 number of surveillance measures. Did  
18 there come a time when Janssen pulled  
19 those together in something that was  
20 called a risk management plan?

21 A. Yes.

22 Q. And that occurred when?

23 A. Well, we had a formal risk  
24 management plan agreement with the FDA to

1 monitor these risks in approximately  
2 2005, but we had a number of these  
3 screens in place even before 2005.

4 Q. So this plan built on  
5 monitoring the company had been doing  
6 before that time?

7 A. Yes.

8 Q. And some of the things you  
9 described, the periodic adverse event  
10 report review, for example, that's  
11 something that is required under FDA  
12 regulations, it would have been done  
13 since 1990?

14 A. That's correct. That's  
15 correct. There are regulatory  
16 requirements over periodic reporting of  
17 adverse events.

18 Q. And you referred to the  
19 reports that you had received from, for  
20 example Pinney Associates, which looked  
21 at, among other things, the -- the degree  
22 to which the company had seen abuse of  
23 the patch that the company had at that  
24 time in 2001?

1           A.       Correct. As part of his  
2       assessment of relative risks of abuse, he  
3       reviewed available data around  
4       information on abuse of the Duragesic  
5       patch up to that point.

6           Q.       And this document that we  
7       have in front of us is a presentation  
8       from 2007?

9           A.       I -- yes, that's the date on  
10      the front page.

11          Q.       And you are listed as the  
12      presenter; is that correct?

13          A.       Correct.

14          Q.       And this gives an overview  
15      of -- well, you tell me generally what's  
16      the overview here?

17          A.       An overview of the  
18      activities within the medical affairs  
19      group to monitor for the safety of our  
20      pain products. But the risk management  
21      plan in general, how we go about  
22      collecting the various streams that would  
23      inform us on the safety of our product  
24      and -- and the process by which we review

1       those data internally and externally.

2               Q.       And further down the  
3       document, is there a description of the  
4       Duragesic risk management plan in  
5       particular?

6               A.       Yes.   There is no page  
7       number, but there is a slide that's  
8       labeled Duragesic (opioid risk management  
9       plan).

10              Q.       And that would be the plan  
11       that was in effect in or around 2007 --

12              A.       Yes.

13              Q.       -- at the time you gave that  
14       presentation?

15              A.       Yes.   It's a -- it's an  
16       overview of that plan.

17              Q.       And I take it those plans  
18       evolved over time.   You mentioned that in  
19       2005 you -- you had an agreement with the  
20       FDA to formalize this; is that right?

21              A.       Yes.

22              Q.       And then did it change over  
23       time as the years went on?

24              A.       It did.   We've spoken

1 already about how the risk management  
2 plan ultimately evolved into a REMS  
3 program, and into -- into a  
4 consortiumwide surveillance program.

5 Q. All right. Well, let's take  
6 a quick look at some of the slides,  
7 starting with the ones that deal with  
8 risk management generally.

9 A. So that's towards the  
10 beginning of the document.

11 Q. That's the beginning of the  
12 plan.

13 A. Okay.

14 Q. Now, you have a -- initial  
15 subscribe -- describes the FDA regulatory  
16 system, and then you have the question,  
17 "But how safe is safe?"

18 What is -- what is the point  
19 that you're making there?

20 A. All drugs have risks  
21 associated with them. Every drug has  
22 adverse events, and you have to assess  
23 those risks against the potential  
24 benefits to determine whether to

1 prescribe or to continue a drug for a  
2 specific patient.

3 Q. All right. If you turn to  
4 the next page, there's a section on  
5 limitations of clinical trials. And I  
6 take it your point here is that there are  
7 limitations of clinical trials on the  
8 subject of assessing risk. Can you  
9 describe what those are and what you're  
10 conveying in this slide?

11 A. Yes. Absolutely. So  
12 clinical trials are conducted in a highly  
13 controlled environment. There are clear  
14 selection criteria, inclusion/exclusion  
15 criteria in a clinical criteria.

16 So by virtue of that highly  
17 controlled environment there are  
18 limitations on the full picture of safety  
19 and efficacy that you might ultimately  
20 develop with a drug.

21 It's been well noted that  
22 even large clinical trials would have  
23 difficulty in determining adverse events  
24 that -- that might be serious but that

1 are seen at a very low incidence in the  
2 general population. That's one of the  
3 limitations on a clinical trial.

4 You're also limited in the  
5 patient population you're seeing. So you  
6 might want -- you might need to develop  
7 more data around an elderly population.  
8 We certainly know of doing separate  
9 studies in a pediatric population. Those  
10 would not necessarily be answered with  
11 the initial clinical trials.

12 Q. If you'll turn to the next  
13 one. This refers to guidance for  
14 industry. What guidance is that  
15 referring to?

16 A. The FDA published in the  
17 federal register a guidance around risk  
18 management.

19 Q. And that came out in 2005?

20 A. Yes.

21 Q. And that was one of the  
22 reasons for systematizing this risk  
23 management plan, I take it?

24 A. That's correct.

1           Q.     Let's move on to -- you can  
2     skip the next slide and go to the slide  
3     entitled "Goals of a Risk Management  
4     Program."

5                     What's the point that you're  
6     making in this slide?

7           A.     So to the extent possible,  
8     we want to -- when I say optimize the  
9     benefit-risk ratio, so by optimizing a  
10    ratio, you can either increase the  
11    positive aspect, the efficacy of the  
12    drug, or you can minimize the risks. So  
13    if you can identify the risks and take  
14    steps to minimize those risks, that works  
15    towards optimizing that benefit-risk  
16    ratio.

17           Q.     And the next slide is  
18    entitled "the process of risk  
19    management." Can you explain that one?

20           A.     Going back to what I just  
21    spoke about. So understand what the  
22    risks are associated with your product  
23    and develop tools so that you can  
24    minimize those risks. And those tools

1 might be education, education for the  
2 healthcare provider, education for the  
3 patient.

4 And as you -- and over time  
5 you may need to change those.

6 Q. Is that what Janssen is  
7 trying to do with the risk management  
8 plan for Duragesic?

9 A. Yes.

10 Q. Next slide is "Tools." Can  
11 you comment on that one, please.

12 A. Yes. These are -- these are  
13 methodologies that might be employed.  
14 I'm not saying necessarily for Duragesic.  
15 But these are some of the tools that  
16 could be used to minimize risks  
17 associated with a product, not just an  
18 opioid.

19 We've spoken about education  
20 and training for the healthcare providers  
21 and educating patients.

22 Just looking at a number of  
23 these, you might restrict the setting in  
24 which the drug might be used so that it

1 would be only within a hospital setting.

2 You might require that  
3 patients register before they could use  
4 the drug or that -- or limit it to  
5 certain types of physicians.

6 Again, this goes across all  
7 drugs where you are considering a risk  
8 management plan.

9 Q. And in the next slide you  
10 have "Evaluating the Plan." And it  
11 speaks of criteria for success, signals,  
12 strategies for intervention. Can you  
13 explain what signals and strategies for  
14 interventions are?

15 A. We would put in surveillance  
16 mechanisms that would help us assess the  
17 identified risks, primarily risks of  
18 abuse, misuse and diversion, but  
19 certainly the adverse events that we've  
20 spoken of, that were common for opioids.

21 And how we would go about  
22 collecting data on the incidence of those  
23 risks and what would constitute a signal  
24 where we might need additional

1 intervention or more information.

2 Q. And what kind of  
3 intervention might that be?

4 A. Interventions might be  
5 changes in our educational material,  
6 changes in the package insert. It might  
7 be, in the case of a surveillance  
8 program, sending someone out or getting  
9 more information about what's going on in  
10 a particular geographic area to  
11 understand the background behind what we  
12 may be seeing in the surveillance  
13 program.

14 Q. All right. Your  
15 presentation goes on to give another --  
16 some examples involving another drug.  
17 Let's go, move forward to the discussion  
18 now of Duragesic risk management plan.

19 And if you turn to the first  
20 slide there, that's a -- I guess a  
21 graphic representation of the way the  
22 plan was organized. Can you just give a  
23 quick summary of what that's supposed to  
24 depict?

1           A.       Yes. We've spoken about  
2 risks and we -- starting with the  
3 understood risks or perceived risks of a  
4 medication, we assess the risks and what  
5 tools we have to manage the risk.

6                   The assessment would be a  
7 variety of data. That might include, in  
8 the case of opioids, abuse liability  
9 studies, epidemiology, in vitro studies,  
10 and then ways in which we could manage  
11 those risks.

12                   Managing those risks could  
13 entail things that we've already spoken  
14 of, appropriate labeling so that the  
15 risks are properly conveyed to the  
16 healthcare provider who's prescribing the  
17 drug; education, both to the healthcare  
18 provider and the treating community,  
19 activities around launch and promotion of  
20 these risks are continued to be brought  
21 to the physicians' attention about the  
22 proper patient selection and monitoring;  
23 surveillance, we've spoken about the  
24 streams of data that come into us that

1 look at issues around abuse, misuse and  
2 diversion; supply chain management, which  
3 we've spoken about; manufacturing which  
4 we've spoken about.

5 Q. So under surveillance,  
6 there's two categories, one is routine or  
7 passive and the other is active. Can you  
8 explain the difference between those two?

9 A. Routine, passive, for the  
10 most part these are the adverse event  
11 reports that come into the company.  
12 We're not going out and soliciting them.  
13 Maybe in the case of a clinical trial we  
14 might be. But these are adverse events  
15 that are reported to us, passive in that  
16 respect -- in that respect.

17 Active being that we are  
18 actively supporting surveillance to  
19 understand what -- how the drugs are  
20 being used in the community and whether  
21 there are issues around abuse, misuse and  
22 diversion.

23 Q. All right. So what were  
24 the -- what were the passive surveillance

1 tools that Janssen had available for  
2 Duragesic?

3 A. Adverse event reporting  
4 would be the primary one, yeah.

5 MR. LIFLAND: Let's take a  
6 look at one of the progress  
7 reports.

8 Does anyone need a break or  
9 are we good?

10 MS. CONROY: Fine.

11 MR. LIFLAND: I'd like to  
12 mark as the next, Exhibit Number  
13 36.

14 (Document marked for  
15 identification as Exhibit  
16 Janssen-Moskovitz-36.)

17 MR. LIFLAND: The document  
18 begins with Bates number  
19 JAN-MS-00213785, and ends with --  
20 oh, I'm sorry, that's -- that's  
21 the number. It's a native file  
22 provided.

23 BY MR. LIFLAND:

24 Q. Doctor, can you look at the

1 title page of this document and tell us  
2 what it is?

3 A. The Duragesic first annual  
4 progress report. This is part of the  
5 periodic safety update that was required  
6 to be filed with the Food and Drug  
7 Administration.

8 Q. So this is a report that's  
9 prepared under the risk management plan,  
10 the first one, in fact?

11 A. It's part of our  
12 responsibility to report adverse events  
13 and -- and the -- and the risk management  
14 activities that we agreed to provide.

15 Q. And the issue date is listed  
16 there as the 5th of June, 2007?

17 A. Yes.

18 MR. RODRIGUEZ: What exhibit  
19 number are we on?

20 MR. LIFLAND: Oh, I'm sorry.

21 MS. CONROY: I'm sure he  
22 said it, I just missed it. I'll  
23 go back --

24 MR. LIFLAND: 36.

1 MS. CONROY: Thank you.

2 BY MR. LIFLAND:

3 Q. So if you turn to the table  
4 of contents you'll see how the report is  
5 structured, correct?

6 A. Correct.

7 Q. It gives you a description  
8 of what the risk management plan is?

9 A. Yes.

10 Q. And what it's looking at?

11 A. Yes.

12 Q. In Section 2, or 1 is the  
13 introduction and the background explains  
14 it?

15 A. That's correct.

16 Q. And then Section 3 goes  
17 through all the elements of the plan and  
18 what the -- what the findings are for  
19 this reporting period; is that correct?

20 A. Yes.

21 Q. All right. And if you turn  
22 to Page 12, there's a summary.

23 A. Executive summary, yes.

24 Q. And the first thing after

1 the introduction is what's referred to as  
2 pharmacovigilance plan?

3 A. Yes.

4 Q. And that I take it is what's  
5 referred to as the passive monitoring or  
6 the passive surveillance?

7 A. Yes.

8 Excuse me.

9 Q. And the next page describes  
10 the elements of that. The first one is  
11 review of the SCEPTRE database.

12 A. Yes.

13 Q. You described the SCEPTRE  
14 database?

15 A. That was the adverse event  
16 reporting database that -- to which we  
17 entered all reports of adverse events on  
18 a worldwide basis.

19 Q. So when you say on a  
20 worldwide basis, there were other  
21 countries in the world in which Janssen  
22 sold fentanyl patches?

23 A. Yes.

24 Q. And so this would compile

1       adverse events not just from the United  
2       States?

3               A.       That's correct.

4               Q.       And those would be analyzed  
5       as the first part of the surveillance?

6               A.       Yes.

7               Q.       And then the second is,  
8       underneath that the FDA SRS/AERS  
9       database. What is that?

10              A.       The FDA also had a database  
11       of adverse events if a healthcare --  
12       healthcare provider or a patient might  
13       report to the FDA and not report to the  
14       company. So there was an attempt to  
15       share the databases so that we had  
16       similar information that we were working  
17       with.

18              Q.       Okay. So the first step in  
19       this place is to do a review of all of  
20       the FDA's adverse events and --

21              A.       And -- FDA and our adverse  
22       events.

23              Q.       And then all of the  
24       company's adverse events that it's

1       learned about worldwide?

2                   A.       Correct.

3                   Q.       Okay. And the next listed  
4       under here is review of the drug abuse  
5       warning network, DAWN.

6                             Can you explain what that  
7       is?

8                   A.       It collects data on  
9       emergency department visits for a variety  
10      of drugs, I mean, but emergency  
11      department visits which are related to  
12      drug intake.

13                  Q.       And what information does  
14      that provide relating to abuse, misuse?

15                  A.       That in the most serious  
16      cases, if the intake of a drug led to the  
17      need to present the patient to an  
18      emergency room, we would have information  
19      on the drugs that were used that led to  
20      that emergency room admission.

21                  Q.       And is that -- who -- who  
22      puts together that data?

23                  A.       There's a separate database  
24      that's maintained by the DAWN group. I

1     don't recall exactly how it is  
2     constructed.

3             Q.     Is it a government database?

4             A.     It is.

5             Q.     Federal domain?

6             A.     Yes.

7             Q.     And then the next on the  
8     list is review of IMS Health LRx  
9     database. Can you explain how that's  
10    used in the risk management plan?

11            A.     Well, this helps us  
12    determine patient exposure to Duragesic  
13    and other compounds.

14            Q.     So it would give you a  
15    baseline of exposure that you could  
16    then --

17            A.     How many prescriptions were  
18    written and how many patients received  
19    the drug.

20            Q.     All right. Then we have a  
21    reference to Poison Control Center data.  
22    And is this -- are we now moving into the  
23    area of active surveillance?

24            A.     Yes. These were streams

1       that we contracted to receive from the  
2       Poison Control Centers.

3               Q.       And have you heard of  
4       RADARS?

5               A.       Yes.

6               Q.       And can you tell us what  
7       that stands for?

8               A.       Research, abuse -- I'd have  
9       to go back on the exact acronym.

10              Q.       It's referred to on the  
11      next -- the next page here. Explain what  
12      it is.

13              A.       Well, there are a number  
14      of -- of surveillance programs that fall  
15      under RADARS. But they -- they monitor  
16      for streams of -- that would help to  
17      detect abuse, misuse and diversion.

18              Q.       And then there's a reference  
19      to National Forensic Laboratory  
20      Information System.

21                      What's that?

22              A.       In instances where samples  
23      might be submitted to a laboratory to  
24      determine what the cause of death was or

1 if there was an adverse event, they would  
2 have a database that they would be able  
3 to determine what the drug was that was  
4 used when it came to the attention of the  
5 laboratory.

6 Q. Further down the page is a  
7 reference to supplemental RADARS program  
8 from the RADARS system.

9 Can you explain what that  
10 is?

11 A. We have the opportunity  
12 to -- to be a little bit more granular  
13 with the data that RADARS provides and to  
14 get down to a three-digit zip code level.  
15 That's the supplementary data.

16 It -- so it -- the elements  
17 of that would include drug diversion  
18 network, key informant network, opioid  
19 dependence treatment network.

20 Q. What's a key informant  
21 network?

22 A. There were individuals in  
23 various geographic locations throughout  
24 the country who had their ear to the

1 ground around issues of abuse, misuse,  
2 diversion, particularly for an illicit  
3 drug that might be coming into the area,  
4 and they would help inform what was going  
5 on.

6 Q. And then finally, there's a  
7 reference, at the top of the next page to  
8 supplementary internet media monitoring  
9 programs?

10 A. Yes.

11 Q. Explain what that is.

12 A. So we would monitor, or we  
13 would contract with a group that would  
14 monitor -- there were sites that were  
15 well known to drug users, abusers on the  
16 internet where they would talk about  
17 their experiences using drugs, what gave  
18 them the high, how easy it was to obtain  
19 the drug -- excuse me.

20 And we were monitoring  
21 those -- these internet sites to gain an  
22 understanding of, especially over time,  
23 what the interest in particular drugs,  
24 particular formulations might be.

1 MR. LIFLAND: Maybe we  
2 should take a quick break. I  
3 think it sounds like you need some  
4 water.

5 THE WITNESS: If you don't  
6 mind. Thank you.

7 THE VIDEOGRAPHER: All  
8 right. Remove your microphones.  
9 The time is 5:20 p.m. Going off  
10 the record.

11 (Short break.)

12 THE VIDEOGRAPHER: We are  
13 back on the record. The time is  
14 5:29 p.m.

15 BY MR. LIFLAND:

16 Q. Dr. Moskovitz, can you turn  
17 to Page 29 of the progress report, risk  
18 management plan progress report that  
19 we've been discussing.

20 THE VIDEOGRAPHER: Your  
21 microphone.

22 THE WITNESS: Mine too.  
23 Sorry.

24 MR. LIFLAND: All three of

1                   us.

2                   MS. CONROY: Yeah.

3 BY MR. LIFLAND:

4                   Q. Dr. Moskovitz, could you  
5 please turn to Page 29 of the risk  
6 management plan progress report that  
7 we've been discussing.

8                   A. Yes.

9                   Q. And the two headings on this  
10 page refer to cumulative reviews of  
11 information from the company's adverse  
12 event database that the company  
13 performed. Do you see those?

14                  A. Yes, I do.

15                  Q. And is that something that  
16 the company would do periodically from  
17 time to time if a question came up?

18                  A. Yes.

19                  Q. And can you tell us what the  
20 first one of those is?

21                  A. 2.6.4?

22                  Q. 2.6.4.

23                  A. Iatrogenic addiction,  
24 addiction that -- that from -- was an

1 outcome of prescribing of Duragesic. So  
2 it was a review of cases of addiction  
3 associated with prescriptions of  
4 addiction -- of Duragesic.

5 Q. So these would be patients  
6 who had received a prescription and  
7 become addicted?

8 A. That is my understanding.

9 MR. LIFLAND: Have we got  
10 the -- I'm going to hand you  
11 another document on this topic.  
12 We'll mark it as -- are we on 37?

13 (Document marked for  
14 identification as Exhibit  
15 Janssen-Moskovitz-37.)

16 THE WITNESS: Do you want me  
17 to keep this here?

18 BY MR. LIFLAND:

19 Q. Yeah, you can keep it there.  
20 We're going to come back to both of  
21 those. I just want to review this.

22 A. Okay.

23 Q. Can you read the title of  
24 this document.

1                   A.       "Cumulative Review of  
2       Iatrogenic Addiction Associated With the  
3       Use of Transdermal Duragesic Fentanyl  
4       Patch."

5                   Q.       And is this a report of that  
6       review that's referred to here in the  
7       risk management plan that we just  
8       discussed?

9                   A.       By the dates, it would  
10      appear to be, yes.

11                  Q.       And can you just take a  
12      moment to look at it and then describe  
13      what the review was?

14                  A.       So going through the  
15      database, based upon the -- our database,  
16      we reviewed all cases that would be  
17      suggestive of iatrogenic addiction  
18      reported to the company with the use of  
19      the transdermal fentanyl patch.

20                  Q.       And for what period of time  
21      would this cover?

22                  A.       Without seeing specifically  
23      the timeline, I would assume this would  
24      be over the entire course of the

1 marketing for Duragesic. That is to say,  
2 from 1990 on.

3 Q. Does it cover just the  
4 United States or is it worldwide?

5 A. This is a worldwide  
6 database.

7 Q. All right. So it's your  
8 understanding that -- then that this is a  
9 review of cases reported worldwide, of  
10 all the cases that have been reported to  
11 the company on cases of what might be  
12 suggestive of iatrogenic addiction with  
13 Duragesic patients on Duragesic?

14 A. Correct.

15 Q. Or the international  
16 versions of it?

17 A. Correct.

18 Q. And can you take a look at  
19 the conclusion of the -- well, let me  
20 start. Is there -- is there a discussion  
21 of the exposure to Duragesic that the  
22 period of time that these cases are drawn  
23 from --

24 A. Yes.

1 Q. -- corresponds to?

2 A. Yes.

3 Q. Page 9?

4 A. Yes. I'm looking at Page 9.

5 And thank you, that helps me determine,  
6 so that it is, in fact, from launch  
7 through June 2005.

8 Q. And what's the -- what's the  
9 amount of exposure that's shown there?

10 A. Well, overall in terms of  
11 patient days, it would be 1,611,000 --  
12 more than a billion patient days.

13 Q. So it's approximately 1.1  
14 billion 600 thousand --

15 A. 1,611,158,440.

16 Q. Okay. But that's  
17 1.6 billion roughly?

18 A. 1.6 billion roughly, yes.

19 Q. And what is a patient day?

20 A. A patient day would be one  
21 day of exposure of a patient to the  
22 Duragesic patch.

23 Q. And if you look at the  
24 conclusion of -- well, just take a look

1 at the results of the conclusion and  
2 maybe you can summarize what the finding  
3 was based on this review.

4 A. That iatrogenic addiction  
5 was very rare.

6 Q. How many cases did they  
7 find?

8 A. They found 103 cases during  
9 this -- over that period of time.

10 Q. All right. If you go back  
11 to the previous document, which is  
12 Exhibit 36 I think.

13 A. Yes.

14 Q. And you'll see underneath  
15 the reference to that study we just saw,  
16 or that review that we just discussed is  
17 another cumulative review of death cases  
18 with the fentanyl transdermal system.

19 Do you see that?

20 A. Yes.

21 Q. And -- and do you recall  
22 that review?

23 A. Yes.

24 Q. Can you explain how that

1       came about and what the result was?

2               A.       So there was an FDA Public  
3       Health Advisory around issues of misuse  
4       of the Duragesic patch and deaths. And  
5       we had a -- the global regulatory had a  
6       request from the German health  
7       authorities to analyze all cases of  
8       Duragesic use where the outcome was death  
9       that was reported to the company.

10              Q.       And probably there's enough  
11       here, if you look at the next page, you  
12       can see the rest of the description of  
13       that. Can you -- does this tell you what  
14       the results of that review was?

15              A.       That most of the cases of  
16       death were expected deaths because the  
17       drug was used in end-of-life conditions,  
18       and that there was no increase, in a  
19       trend in increase in reporting rates of  
20       death between the year 2000 and 2005.

21              Q.       And when you say expected  
22       deaths, you're referring to a situation  
23       where for example, a person might be  
24       taking Duragesic to relieve pain from

1 terminal cancer and they die while they  
2 are on the -- on the medicine, but the  
3 cause of death is not the medicine, it's  
4 the cancer. Is that what you're  
5 referring to as an expected death?

6 A. That's correct, where the  
7 reporter did not attribute the death to  
8 the Duragesic patch.

9 Q. And again the conclusion  
10 with respect to deaths that did not fall  
11 into category -- into that category, was  
12 what?

13 A. That we didn't -- that there  
14 was no trend to suggest an increase in  
15 the death rate, and, therefore, the --  
16 the core data sheet adequately describes  
17 those risks, the risk of death with the  
18 drug.

19 Q. And what's the core data  
20 sheet?

21 A. The company core data sheet  
22 is a worldwide document that contains all  
23 the information about the drug. And  
24 based upon the company core data sheet,

1 the individual package inserts would be  
2 harmonized to the company core data  
3 sheets. There might be differences from  
4 one region to another. But it contains  
5 the -- the fundamental information that  
6 has to be included in all package  
7 inserts.

8 Q. Let's go back to the slide  
9 presentation on the risk management plan.  
10 I think it will be easier to use this  
11 document just to walk through the last  
12 few pieces of it.

13 A. Okay.

14 Q. And what I'd like to do is,  
15 let's move forward to the sections of the  
16 document that report on the findings of  
17 the data, the data from the latest plan.  
18 It gives some examples.

19 So if you can turn to the  
20 page that says, "Passive Surveillance:  
21 Data" -- "Databases routinely surveyed."

22 A. Yes.

23 Q. And those are some of the  
24 ones -- well, let's go back to the prior

1 page. There's a reference to routine  
2 surveillance. That's the SCEPTRE and  
3 the -- and the FDA AERS that we talked  
4 about --

5 A. Yes.

6 Q. -- right?

7 A. Yes.

8 Q. And then the next page  
9 refers to some of the other passive  
10 surveillance databases. The DAWN  
11 database that you mentioned.

12 A. There's additional streams  
13 of data that we were collecting about  
14 specific issues of abuse, misuse,  
15 diversion, of fentanyl and other  
16 products.

17 Q. Right. So DAWN was the  
18 emergency room mentions?

19 A. Yes.

20 Q. And there's a reference to  
21 toxic exposure surveillance system,  
22 abbreviated TESS. What's that?

23 A. I'd have to go to another  
24 document to refresh my memory about what

1       TESS was.

2                   Q.       Poison control?

3                   A.       Well, since poison control  
4       isn't listed over here and I know that we  
5       did it, my assumption is that that's what  
6       it's referring to.

7                   Q.       And then the National  
8       Forensic Laboratory Information Service  
9       we talked about, right?

10                  A.       Yes.

11                  Q.       And the IMS database?

12                  A.       Database that helped us  
13       assess exposure.

14                  Q.       And the next page actually  
15       has a table that lists what aspects of  
16       what you're surveying, what you're  
17       looking for, each of these databases  
18       would give you information about,  
19       that's -- is that correct?

20                  A.       That's correct.

21                  Q.       So for diversion, you have  
22       information from the J&J SCEPTRE, from  
23       the FDA, and from the National Forensic  
24       Labs?

1 A. Yes.

2 Q. For misuse -- well, the J&J  
3 SCEPTRE and the FDA covers information on  
4 all of these adverse --

5 A. All of those --

6 Q. -- abuse, overdose, misuse,  
7 diversion, other adverse events, correct?

8 A. Adverse events of interest.

9 Q. Right.

10 A. That's correct.

11 Q. And then TESS speaks to  
12 abuse, overdose and misuse?

13 A. Yes.

14 Q. NFLIS, diversion?

15 A. Diversion.

16 Q. IMS?

17 A. Misuse.

18 Q. Misuse.

19 And then DAWN would be?

20 A. Overdose and abuse.

21 Q. And then if you go to the  
22 next page we get into the active  
23 surveillance tools, correct?

24 A. Correct.

1 Q. It starts off with RADARS?

2 A. Yes.

3 Q. It still doesn't say what  
4 RADARS stands for, but I assume we'll --  
5 at some point, we'll come across that.

6 And --

7 A. It's research, abuse.

8 That's definitely the R and A --

9 diversion activities. I --

10 Q. Let me -- let me ask you the  
11 question. Who ran RADARS?

12 A. Well, initially it was the  
13 Rocky Mountain Control Group that -- Rick  
14 Dart's group in Colorado ran RADARS.

15 Q. So that was an independent  
16 group of experts who set up this  
17 surveillance network?

18 A. That's correct.

19 Q. And it lists here four  
20 different networks?

21 A. Yes.

22 Q. So within RADARS you had the  
23 four different sources that you could  
24 look to for different kinds of data that

1 speak to the questions you're looking  
2 for?

3 A. Yes. Four different streams  
4 of information that came in.

5 Q. Okay. And let's look at the  
6 first one. This is key informant data.  
7 This is one of the RADARS data streams I  
8 take it?

9 A. Yes.

10 Q. And can you describe again  
11 what that is?

12 A. There -- there were  
13 individuals in geographic areas  
14 throughout the country who would alert  
15 the company to -- well, alert RADARS  
16 about issues of abuse, misuse of -- and  
17 diversion of a variety of compounds  
18 within their geographic area.

19 Q. And this particular table is  
20 showing their data from 2002 through the  
21 first part of 2005; is that correct?

22 A. That's correct.

23 Q. It lists the number of cases  
24 that are reported out of this key

1 enforcement network --

2 A. Informant.

3 Q. -- informant network --

4 A. Yes.

5 Q. -- for a bunch of different  
6 opioids, correct?

7 A. Yes.

8 Q. And fentanyl is one of them,  
9 correct?

10 A. Yes.

11 Q. Is that Duragesic only?

12 A. No. This would be any  
13 mention of fentanyl.

14 Q. So it could be Duragesic in  
15 part?

16 A. It could be Duragesic. It  
17 could be --

18 Q. What else could it be?

19 A. It could be another  
20 formulation of Duragesic, including at  
21 this time the buccal formulations of  
22 fentanyl.

23 Q. Right. You said another  
24 formulation of Duragesic.

1           A.       I'm sorry. Another  
2       formulation of fentanyl, which could  
3       include the buccal formulations. Actiq  
4       was one that was -- by brand name.

5           Q.       And just for my benefit,  
6       what does buccal mean?

7           A.       Oh, it's placed in the mouth  
8       sublingually so that you have a rapid  
9       absorption of the fentanyl.

10          Q.       So it's a lozenge that you  
11       place under your tongue, and it's  
12       absorbed that way?

13          A.       Absorbed quickly.

14          Q.       So that was a product by  
15       another company -- marketed by another  
16       company. It was another fentanyl  
17       product.

18          A.       Yes.

19          Q.       And could these mentions be  
20       anything else?

21          A.       It could be illicit fentanyl  
22       mentions as well.

23          Q.       So all of those would be  
24       combined in the fentanyl line in this

1 data?

2 A. Yes.

3 Q. Okay. Can you see which  
4 line here is the fentanyl line?

5 A. Yes. Thankfully it's in  
6 color. The green line represents the  
7 fentanyl cases.

8 Q. So, and I know it's a little  
9 hard to see. But if I point to it with  
10 my pen, it's this green line right here  
11 that -- it looks like for most of this  
12 period, it's close to the bottom.  
13 There's one that, it looks like  
14 buprenorphine is a little bit lower?

15 A. Yeah, it's the lowest or  
16 second lowest except for one data point  
17 before all the other data points.

18 Q. And it's considerably lower  
19 than the data points for the other  
20 product, at least some of the other  
21 products mentioned, really all of them  
22 except for that one that's lower,  
23 correct?

24 A. That's correct.

1           Q.     All right. Let's go to the  
2     next slide. This is the law enforcement  
3     network data, drug diversion total  
4     mentions 2000, 2004. And this is another  
5     RADARS resource, correct?

6           A.     Correct. Seizures of  
7     medications that may have been illicitly  
8     diverted outside the normal prescription  
9     stream.

10          Q.     And again, fentanyl is the  
11     green line?

12          A.     Yes.

13          Q.     And fentanyl here could  
14     include --

15          A.     Hold on. Hold on. Fentanyl  
16     is the dark green line here. Diazepam is  
17     also green, but fentanyl is a darker  
18     green.

19          Q.     Okay. Dark green with the  
20     triangles. And -- well, I'll take a  
21     minute.

22          A.     And again, fentanyl is among  
23     the lowest mentioned.

24          Q.     And just to confirm, would

1 the same be true that fentanyl on this  
2 chart would include not only any mentions  
3 that they found for the Duragesic patch,  
4 but also illegal fentanyl, which could  
5 have been seized by law enforcement?

6 A. And other formulations of  
7 fentanyl. That's my understanding.

8 Q. Let's look at the next  
9 chart. This is AATOD report. Maybe we  
10 can go back and refresh on what that  
11 stands for. American Association For the  
12 Treatment of Opioid Dependence?

13 A. It's my understanding that  
14 this is a database for patients who were  
15 admitted to methadone treatment programs,  
16 and they would report on the drug that  
17 they had taken -- abused most recently  
18 during the prior month, prior to their  
19 admission to the methadone treatment  
20 program.

21 Q. All right. If we look at  
22 this chart, the top one is heroin?

23 A. Yes.

24 Q. And then next we have some

1 of the more commonly prescribed opioid  
2 pills?

3 A. Yes.

4 Q. And where is fentanyl on the  
5 chart?

6 A. It's the third from the  
7 bottom.

8 Q. So it's this one that I'm  
9 pointing to right now?

10 A. Yes.

11 Q. Okay. And again, those  
12 would include Duragesic, any other forms  
13 of fentanyl altogether, correct?

14 A. Again, that's my  
15 understanding, yes.

16 Q. Now, taking a look at this  
17 chart, this is a chart which isn't  
18 breaking out different opioid drugs. Can  
19 you tell us what this is showing?

20 A. Yeah. So this is -- so in  
21 the previous slide we've spoken about the  
22 drugs they would have -- they reported  
23 taking in the month prior to the  
24 admission to the methadone treatment

1 clinic. Here we're looking at where  
2 their source of those drugs was, from  
3 where they received the drugs that they  
4 were abusing.

5 Q. And some of those -- I'm  
6 pointing right here -- are from  
7 prescriptions that they got, according to  
8 what they reported, correct?

9 A. Yes.

10 Q. But there are two categories  
11 that are even higher than that. What are  
12 those two categories?

13 A. From a drug dealer,  
14 80 percent of the individuals admitted to  
15 the methadone treatment program; or from  
16 a friend or relative, more than  
17 50 percent of the patients received drug  
18 from a friend or relative.

19 These are -- these don't add  
20 up to 100, because there may have been  
21 more than one source for the drug.

22 Q. So if you're receiving from  
23 a friend or relative, that's not -- that  
24 would be -- fall into the category of

1 potentially both -- well, certainly  
2 misuse and abuse, both, right?

3 A. Well, certainly misuse.  
4 You're not prescribed the product. So  
5 you're not taking it for the prescribed  
6 analgesic effect.

7 Q. The next slide is just  
8 showing the poison -- the parts of the  
9 country that the Poison Control Center  
10 data is covering, right?

11 A. That's correct.

12 Q. So let's get to the next  
13 chart. And we have "Poison Control  
14 Center data: Intentional exposure rates  
15 by quarter."

16 And, again, this goes  
17 through -- I guess it starts in '03 and  
18 goes to the second quarter of '05. Can  
19 you explain what that is?

20 A. So they were monitoring --  
21 I'd have to go back to what they mean by  
22 "intentional exposure." I think these  
23 are cases where it became known to RADARS  
24 through their stream where the patient --

1 where the individual took a drug of abuse  
2 over this period of time. And came to  
3 the -- well, the Poison Control Center  
4 was the head center for RADARS.

5 So I don't know which stream  
6 they're reporting on for this specific  
7 dataset.

8 Q. And where is fentanyl on  
9 this chart? Can you see?

10 A. Yes. Fentanyl is, across  
11 this period of time, the third from the  
12 bottom.

13 Q. So it's, again, the green  
14 line that I am pointing to that's near  
15 the bottom?

16 A. Yes.

17 Q. And again, this is  
18 potentially any form of fentanyl,  
19 including illegal?

20 A. Yes.

21 Q. Now, the next chart is some  
22 zip code-specific data. Did -- do you  
23 know whether this chart refers to actual  
24 data from a Duragesic report or whether

1 it's simply an example of what this data  
2 collects?

3 A. My best recollection,  
4 particularly looking at these data today,  
5 is that we're talking about rates of  
6 exposure for hydrocodone, and that's what  
7 the "HC" is.

8 Q. And -- but you did have this  
9 information for Duragesic as part of the  
10 service that the company contracted with  
11 RADARS to provide?

12 A. Yes.

13 Q. And when you saw zip  
14 code-level data, what typically, if you  
15 remember, what numbers of cases would you  
16 typically see in those reports?

17 A. Very low. You either saw no  
18 cases in a three-digit zip code or one to  
19 three cases in a three-digit zip code.

20 Q. And if you saw, let's say,  
21 three cases, what would -- would action  
22 be taken?

23 A. There were boundaries.  
24 There were certain set points at which

1     there would be an intervention to further  
2     explore what the -- what was going on in  
3     that three-digit zip code. It would  
4     depend not just upon the three-digit zip  
5     code, but whether activity was seen in  
6     adjacent three-digit ZIP codes or whether  
7     we saw this activity for more than one  
8     quarter.

9                     So if it met certain  
10    criteria for -- certain surveillance  
11    criteria, we would explore further. And  
12    that might include calls to the area, to  
13    legal -- to the police in the area or  
14    representatives who are following up on  
15    issues, legal issues of policing, or  
16    actually send somebody down to try to  
17    understand the environment in that area.

18                    Q.     And who actually would do  
19    that work?

20                    A.     Someone from RADARS.

21                    Q.     Can we take a look at the  
22    next slide. Does this ring a bell with  
23    you?

24                    A.     Yes.

1           Q.     Can you describe what  
2     happened here?

3           A.     So this is an example where  
4     reports of fentanyl increased to the  
5     point where we did further investigation  
6     of what was going on to understand the  
7     mentions of fentanyl in a three-digit zip  
8     code.

9                     And so in 2006, we learned  
10    of addicts who were dying of heroin  
11    overdoses, but the heroin was tainted  
12    with fentanyl. And we were exploring  
13    whether the fentanyl that was found in  
14    blood -- in the laboratory testing of the  
15    blood might have come from pharmaceutical  
16    grade Duragesic. So we did a deeper  
17    dive, if you will, to try to understand  
18    that.

19                    Ultimately RADARS dispatched  
20    a -- a Drug Enforcement Agency agent to  
21    investigate on our behalf, and we learned  
22    that the fentanyl that was -- that was  
23    mixed in with the heroin that was leading  
24    to these deaths, in fact, came from an

1 illicit source. It was from a -- a  
2 laboratory in Mexico and was not --  
3 Duragesic was not the source of the  
4 fentanyl.

5 Q. Let's go back to the slide  
6 that's entitled Proposed Review For  
7 Interventions.

8 A. I have that.

9 Q. And I take it this is  
10 discussing how the company would address  
11 issues that potentially could be picked  
12 up in the surveillance plan like the one  
13 that we just saw, correct?

14 A. Yes, proposed interventions  
15 and -- and how we would evaluate the data  
16 streams that were coming into us from  
17 these surveillance systems.

18 Q. And there is a reference  
19 here to project RMT, or product RMT. I'm  
20 sorry. Can you tell us what that is?

21 A. Product risk management  
22 team. So it was representatives of -- I  
23 think we have -- we may have a slide, but  
24 it would include representatives from the

1 regulatory group, from the safety group  
2 that -- that made the report, from legal,  
3 from sales management, from medical  
4 affairs, a cross-functional team that --  
5 that evaluated these data streams.

6 Q. And as a result of  
7 evaluation the team might recommend the  
8 changes that are referenced here. Could  
9 you explain those?

10 A. So as a result of the  
11 findings of these surveillance streams,  
12 we might recommend that we change  
13 labeling or that we increase or change  
14 our educational efforts. Change our  
15 sales training materials and promotional  
16 materials, or notify the supply chain  
17 group about activity that we uncovered.

18 Q. All right. And how often  
19 did these -- this team meet to review the  
20 surveillance data?

21 And let me ask you first,  
22 were you a part of that team?

23 A. I or a member of my team.  
24 It might have been Gary Vorsanger as my

1 representative to that team.

2 Q. And how often were these  
3 meetings held?

4 A. I believe these meetings  
5 were on a quarterly basis initially. I  
6 don't know if that frequency changed.

7 Q. And if you turn the page to  
8 the next slide. This identifies the  
9 areas within the company that had  
10 representatives who would be reviewing  
11 this risk management surveillance data;  
12 is that right?

13 A. No. So -- so --

14 Q. This is a team?

15 A. Right. The risk management  
16 team is separate. The risk management  
17 team we've spoken about. We made a  
18 presentation based upon the data, to  
19 senior management, to the -- the senior  
20 management of these groups that were  
21 involved in the day-to-day -- in the  
22 quarterly review or the assessment of the  
23 data streams. So this was a senior  
24 management level that would include the

1 chairperson of the risk management team,  
2 the safety group, benefit/risk  
3 management, regulatory affairs, medical  
4 affairs, brand, the R&D side,  
5 pharmaceutical group, strategic  
6 management and legal.

7 Q. So the -- the results of  
8 this surveillance were reported up to  
9 senior management?

10 A. To senior management.

11 Q. And of course --

12 A. With our recommendations.

13 Q. And were also reported to  
14 the FDA as we saw in the progress report?

15 A. That's correct.

16 Q. You mentioned earlier that  
17 the Duragesic patch -- that that generic  
18 versions of patch came into market in  
19 early 2005; is that right?

20 A. Yes.

21 Q. And that's because Janssen's  
22 patent for the product expired, so  
23 generics were allowed to come in?

24 A. Quite simply because the FDA

1 approved a generic version of the  
2 Duragesic patch.

3 Q. And did Duragesic become a  
4 smaller and smaller market share in terms  
5 of the number of prescriptions written  
6 compared to the generics after that?

7 A. From 2005 on, yes.

8 Q. And did there come a time  
9 when the company, in fact, stopped  
10 actively promoting it? And I mean in the  
11 sense of no longer sending sales reps out  
12 at all to call on physicians.

13 A. Yes.

14 MS. CONROY: Objection.

15 BY MR. LIFLAND:

16 Q. Do you know approximately  
17 when that was?

18 A. Approximately 2008.

19 Q. All right. Did the company  
20 continue the risk management plan after  
21 it was no longer actively promoting the  
22 product?

23 A. Yes.

24 Q. And why was that?

1           A.       Well, for one thing we had  
2       an obligation under our regulatory  
3       requirements to the FDA, as the NDA  
4       holder, those were commitments that we --  
5       that we made to continue surveillance of  
6       our product.

7           Q.       And I think we saw earlier,  
8       the last one of the progress reports is  
9       from 2012; is that correct?

10          A.       Correct.

11          Q.       And then what happened to  
12       the surveillance after that?

13          A.       Well, in a broad sense  
14       the -- the FDA had already moved to a  
15       determination that the long-acting  
16       opioids should have a risk evaluation  
17       mitigation strategy, REMS program, that  
18       was standard for all of the long-acting  
19       opioids. So we were part of a consortium  
20       that put together the REMS program for  
21       long-acting opioids.

22                   And ultimately the -- the  
23       REMS program and the surveillance program  
24       that was associated with that REMS

1 program was approved by the FDA and that  
2 became the -- the data stream that was  
3 fed to the FDA in lieu of the risk  
4 management plan.

5 Q. All right. I'd like to  
6 change subjects here. We've been talking  
7 really about Duragesic so far. But I  
8 wanted to ask you about the other  
9 Schedule II opioid that we mentioned at  
10 the beginning, which were the tapentadol  
11 products.

12 So when were those products  
13 developed?

14 A. The tapentadol immediate  
15 release began development in the early  
16 2000s, eventually leading to approval in  
17 the United States in 2009. The  
18 extended-release product was developed  
19 later on, eventually leading to approval  
20 in 2011 I believe.

21 Q. And what are the -- what are  
22 the brand names of those tapentadol  
23 products?

24 A. Nucynta and Nucynta ER,

1 extended release.

2 Q. And tapentadol, I take it,  
3 is the chemical name of the molecule  
4 that -- the pain molecule?

5 A. That's correct.

6 Q. And what is tapentadol?

7 A. Tapentadol is a innovative  
8 opioid product that had more than one  
9 mechanism of action that led to its  
10 analgesic effect. So on the one hand, it  
11 was a mu opioid agonist, which is to say  
12 that it -- it bound to the -- the mu  
13 opioid receptor and by virtue of that,  
14 had analgesic properties.

15 But there was a second  
16 mechanism of action which was  
17 norepinephrine reuptake inhibition which  
18 was another mechanism of action  
19 associated with analgesic properties.

20 Q. So part of the analgesic  
21 from the molecule was essentially the  
22 same -- the same route as your typical  
23 long -- well, your typical opioid drug,  
24 the mu agonistic receptor --

1 A. Correct.

2 Q. -- so in that respect it was  
3 an opioid?

4 A. In that respect, it was --  
5 it acted as an opioid.

6 Q. And what you -- you  
7 described as the other pathway, the  
8 norepinephrine reuptake inhibitor, are  
9 there other drugs that people know about  
10 that that would --

11 A. Yes. Antidepressants have  
12 norepinephrine reuptake inhibition.  
13 There are other drugs that use  
14 epinephrine or norepinephrine reuptake  
15 inhibition to -- that can be used for  
16 analgesic properties.

17 Q. And when you say that, they  
18 can be used for pain relief?

19 A. That's correct.

20 Q. And so those -- that was the  
21 molecule that went into -- was the active  
22 ingredient of Nucynta and Nucynta ER  
23 which were the brand names, correct?

24 A. That's correct.

1           Q.       Now, what was the benefit,  
2       maybe it was a hypothetical benefit, but  
3       what was the benefit, hoped-for benefit  
4       of the dual mechanism of action, what was  
5       important about that for the company?

6           A.       We learned early on from  
7       animal models and from preclinical models  
8       that by virtue of having more than one  
9       mechanism of action, a second mechanism  
10      of action that was not mediated through  
11      mu opioid agonism, that there was the  
12      potential to achieve pain relief,  
13      analgesia effect, without some of the  
14      associated side effects of a pure mu  
15      opioid agonist such as Oxycodone or  
16      hydromorphone -- or hydromorphone.

17          Q.       And what were the potential  
18      benefits of that in terms of a pain  
19      relief product?

20          A.       If you could achieve similar  
21      pain relief, the most worrisome side  
22      effects of treating with a potent opioid,  
23      the side effects that would lead most  
24      often to discontinuing an opioid

1 medication, would include  
2 gastrointestinal side effects, nausea,  
3 vomiting, constipation, and some other  
4 side effects, worrisome side effects such  
5 as itching, pruritis.

6 And so by using a drug with  
7 a dual mechanism of action, we would  
8 expect to have a better adverse event  
9 profile.

10 Other potential benefits  
11 were to look at pain models where the  
12 norepinephrine reuptake inhibition was  
13 understood to play a more prominent role  
14 in achieving the level of pain relief.  
15 And that would be in models of  
16 neuropathic pain, probably the best known  
17 model would be diabetic neuropathy.

18 Q. And did the company study  
19 the drug to see if it would be effective  
20 in that specific indication?

21 A. Yes, it did.

22 Q. And what happened with that?

23 A. Ultimately, we had two  
24 adequate, well-controlled trials in a

1     neuropathic pain model, and we -- that  
2     led to the FDA to give an indication of  
3     neuropathic pain for Nucynta  
4     extended-release, Nucynta ER, as well as  
5     the indication of chronic pain. I  
6     believe it was the first opioid to get  
7     that indication.

8             Q.     Now, you said that Nucynta  
9     ER, the one that came in 2011, you said  
10    as well is an indication for chronic  
11    pain. So is that the initial indication,  
12    chronic pain?

13            A.     The initial indication was  
14    for moderate to severe chronic pain.

15            Q.     And was it the same  
16    indication as Duragesic with the other --  
17    the other aspects of it that we  
18    discussed, need around -- you need  
19    around-the-clock pain relief and other  
20    methods of treating it were not  
21    effective?

22            A.     Yes. So as a matter of fact  
23    it was the same indication that I believe  
24    all of the extended-release opioids had,

1     which was for persistent,  
2     around-the-clock, moderate to severe  
3     chronic pain that could not be managed  
4     with a short-acting opioid or other  
5     modalities.

6             Q.     Okay.    So Nucynta  
7     extended-release had that indication, and  
8     then as an additional indication specific  
9     for diabetic -- pain from diabetic  
10    peripheral neuropathy, the neuropathic --

11            A.     Neuropathic pain.

12            Q.     And what about Nucynta IR?  
13    Or I guess it was called Nucynta without  
14    an ER.

15            A.     That's correct.

16            Q.     That was the immediate  
17    release version?

18            A.     That was the immediate  
19    release version.

20            Q.     What was the indication for  
21    that?

22            A.     For acute pain that needed  
23    to be managed with a potent opioid.

24            Q.     And let me ask you again

1 some of the same questions that I asked  
2 on Duragesic.

3 Were there steps the company  
4 took in terms of the product design to  
5 try to make it safer to use with regard  
6 to the risks, the opioid-type risks of  
7 abuse and misuse and diversion?

8 A. Yes.

9 Q. Can you describe that? And  
10 let's start with the product design.

11 A. Well, let me start even  
12 earlier than product design --

13 Q. Okay.

14 A. -- with the basic molecule.  
15 Because it has a dual mechanism of action  
16 and doesn't rely solely upon mu opioid  
17 agonism, there was the hypothesis that,  
18 therefore, it would be less attractive to  
19 someone who is looking to abuse or misuse  
20 the drug.

21 In terms of the design of  
22 the formulation, we're talking here with  
23 the extended-release where higher dose is  
24 delivered. From the outset, the marketed

1 product was developed to be an abuse  
2 deterrent formulation, a formulation that  
3 if you tried to defeat the properties  
4 that led to extended-release, it would be  
5 difficult to defeat those -- those  
6 properties.

7 Q. Now, did you -- what kind of  
8 testing did the company do with regard to  
9 the abuse deterrent formulation?

10 A. Well, we looked at the  
11 physical chemical properties of the  
12 abused deterrent formulation. There were  
13 a whole variety of tests. We used  
14 solvents to try to extract it. Chewing.  
15 We put it in a blender to try to make  
16 smaller pieces. We tried crushing it.

17 Q. What happened in the  
18 blender?

19 A. We broke the blades of the  
20 blender. I remember distinctly seeing  
21 the video of that test.

22 Q. All right. So you had these  
23 tests. Was the company able to label the  
24 product as abuse-deterrent in the way

1       that some of the other opioid products  
2       have been labeled in recent years?

3               A.       No.

4               Q.       And can you explain why not?

5               A.       At the time the drug was  
6       approved, there were other opioid  
7       compounds that were marketed in a  
8       formulation that we would consider to be  
9       abuse-deterrent. It was more difficult  
10      to -- in it was more difficult to defeat  
11      the extended-release properties of the  
12      compound.

13                      The FDA made it clear in an  
14      advisory meeting, I think perhaps more  
15      than one, that they were not -- they  
16      would not allow for a labeling of product  
17      as abuse-deterrent or abuse-resistant  
18      purely on the basis of the physical  
19      chemistry of the formulation, but that  
20      actual data would have to be developed to  
21      show that the formulation would in fact  
22      reduce the rates of abuse, misuse,  
23      diversion because of the abuse-deterrent  
24      properties of the formulation.

1                   So we did not have wording  
2     around that when we brought Nucynta ER to  
3     market.

4                   Q.     And was that data that could  
5     have been developed in the Nucynta ER  
6     clinical trials?

7                   A.     The pivotal clinical trials,  
8     no. Those data would have to be  
9     developed over an extended period of  
10    time, not over the period of a short  
11    trial.

12                  Q.     Okay. But when you brought  
13    the product to market, it still was in  
14    the abuse-deterrent formulation,  
15    regardless of whether you were allowed to  
16    label it as such?

17                  A.     That's correct. In fact,  
18    the clinical trials that we performed  
19    with Nucynta were performed with an  
20    earlier version of the formulation that  
21    was not in an abuse-deterrent  
22    formulation. But we made it clear to our  
23    partner in the development, Grünenthal  
24    Pharmaceuticals, that we would not bring

1 a non-abuse-deterrent formulation to the  
2 U.S. market.

3 So we would wait until the  
4 final formulation with the  
5 abuse-deterrent properties. The  
6 development on that was finished in that  
7 we could do the bioequivalence studies to  
8 show it was bioequivalent to the  
9 formulation that was used in the pivotal  
10 trials.

11 Q. Now, were there other steps  
12 that the company took to assess abuse,  
13 misuse, deterrence in terms of  
14 surveillance for the Nucynta product?

15 A. Yes. We had a risk  
16 management plan that we put in place that  
17 essentially monitored similar data  
18 streams that were already in place for  
19 our Duragesic product.

20 Q. So those would be the ones  
21 we just discussed, the SCEPTRE review,  
22 the FDA AERS review, the various --

23 A. The RADARS program.

24 Q. The RADARS programs, the

1 DAWN. And all of the things essentially  
2 that we just talked about that were  
3 elements of the RADARS risk management  
4 plan were put into the Nucynta risk  
5 management plans?

6 A. That's correct. We -- the  
7 surveillance programs, in a broad sense,  
8 looked at Schedule II opioids. And  
9 Nucynta was a Schedule II opioid. So it  
10 was proven to include it once we began  
11 marketing in established programs that  
12 were monitoring for abuse, misuse,  
13 diversion of these Schedule II products.

14 Q. Have you heard of a  
15 surveillance tool called NAVIPPRO?

16 A. Yes.

17 Q. What is NAVIPPRO?

18 A. NAVIPPRO is a more  
19 sophisticated tool to monitor internet  
20 mentions and publications mentions of  
21 drugs that are abused, misused and  
22 diverted.

23 They -- in addition to the  
24 internet monitoring, they have

1 methodology that can give a more  
2 qualitative in addition to quantitative  
3 assessment.

4 Q. And we haven't mentioned yet  
5 the -- the Nucynta package insert. But I  
6 take it there was a package insert which  
7 gave similar instructions that we talked  
8 about, from Duragesic, about patient  
9 selection, dosing, patient monitoring,  
10 patient counseling, and warnings about  
11 the risks; is that correct?

12 A. That's correct. At this  
13 time, to the degree possible the FDA had  
14 moved to have similar indications,  
15 warnings, instructions to physicians  
16 across all of the long-acting opioid  
17 products. And to the degree that they  
18 could have a similar package insert to  
19 the other long-acting opioids, that was  
20 the package insert that was reflected for  
21 Nucynta ER.

22 Q. Was there -- well, before we  
23 go further on the package insert, let's  
24 just finish up on the surveillance

1 program. And I had asked you about  
2 NAVIPPRO. I want to hand you another  
3 document which is one of the progress  
4 reports for -- progress reports for the  
5 Nucynta ER surveillance plan.

6 (Document marked for  
7 identification as Exhibit  
8 Janssen-Moskovitz-38.)

9 MS. CONROY: What's that  
10 number?

11 MR. LIFLAND: I'm sorry,  
12 what's the number?

13 THE WITNESS: 38.

14 MR. LIFLAND: 38.

15 MS. CONROY: Thank you.

16 BY MR. LIFLAND:

17 Q. If you turn to the first  
18 page I think you'll see that the  
19 nomenclature was changed from the  
20 Duragesic plan which was called the risk  
21 management plan. The title of this one  
22 is surveillance plan --

23 A. Safety surveillance plan.

24 Q. But is it -- it's

1 functionally the same type of safety  
2 surveillance program as what we looked at  
3 before?

4 A. And this is in -- in  
5 December of 2013, I had retired at that  
6 time. But if I look at the table of  
7 contents, the data streams that inform  
8 this safety surveillance were similar to  
9 what had been reported for Duragesic.  
10 There were some specific adverse events  
11 of interest that were specific to Nucynta  
12 such as the serotonin syndrome. But  
13 otherwise similar in breadth to what  
14 we've seen for Duragesic.

15 Q. And if you turn to Page 80.  
16 You can see at the bottom of Page 80 and  
17 then going onto Page 81, a reference to  
18 the NAVIPPRO system programs. And that's  
19 something you were familiar with when you  
20 were still at the company, correct?

21 A. Yes, we began using NAVIPPRO  
22 for Duragesic.

23 Q. And can you -- can you  
24 describe what the NAVIPPRO program was,

1 surveillance program?

2 A. Just reading through the  
3 materials here, surveillance and  
4 interventional programs that analyze data  
5 from three sources, the addiction survey  
6 index multi media version, comprehensive  
7 health assessment for teams, and a web  
8 informed services, internet monitoring,  
9 archive indicators of prescription opioid  
10 medication abuse.

11 Q. And what was the type of  
12 information you were looking for here in  
13 practical terms?

14 A. We wanted early information  
15 on whether tapentadol, the active  
16 ingredient in Nucynta, was going to be  
17 found attractive by drug abusers,  
18 attractive for abuse, misuse and  
19 diversion. This was an opportunity to  
20 explore these issues with a brand-new  
21 opioid product brought to market and to  
22 understand that at a very early stage  
23 through these mechanisms of -- of  
24 internet monitoring and use among

1 teenagers, whether there were concerns  
2 about Nucynta that it might be different  
3 from other opioids.

4 Q. And do you remember what  
5 kinds of data the company received from  
6 the surveillance plans that were put in  
7 place for the Nucynta product?

8 A. That in general, Nucynta was  
9 not a product that was sought by  
10 individuals who would abuse, misuse and  
11 divert -- and divert opioid products.

12 Q. And where did it rank in  
13 terms of the various RADARS indexes that  
14 we looked at on the slide?

15 A. Consistently at the bottom,  
16 or very near the bottom of measures of  
17 abuse, misuse and diversion.

18 Q. Now, when Nucynta, the  
19 extended release was brought out, was  
20 there -- was the extended release, the  
21 class REMS in place yet?

22 A. No. It was still -- it  
23 still hadn't been finalized between the  
24 consortium of companies marketing

1 extended-release products and the FDA.

2 Q. And so did the -- what did  
3 the company do about that?

4 A. We developed a REMS program  
5 similar to the Duragesic REMS program  
6 that we could institute before there was  
7 a final long-acting opioid REMS program  
8 approved for all of the long-acting  
9 opioids.

10 Q. So you put up, when you  
11 introduced the extended-release version,  
12 you had its own REMS to go along with the  
13 launch of the product?

14 A. That's correct. With the  
15 understanding that when there was a REMS  
16 that was approved for all of the  
17 long-acting opioids, Nucynta would be  
18 included as part of that REMS. But we  
19 didn't wait for that. We -- we had a  
20 REMS program earlier.

21 Q. And let me mark the next in  
22 order as Exhibit 39.

23 (Document marked for  
24 identification as Exhibit

1 Janssen-Moskovitz-39.)

2 MS. CONROY: Thank you.

3 BY MR. LIFLAND:

4 Q. Take a moment to flip  
5 through that. Can you tell me what this  
6 document is?

7 A. This is the REMS program,  
8 the risk evaluation mitigation strategy  
9 program per FDA guidelines around the  
10 REMS program that was instituted for  
11 Nucynta ER at the time of launch.

12 Q. And this was in addition to  
13 the safety surveillance plan that we just  
14 looked at?

15 A. That's correct.

16 Q. And what were the elements  
17 of this?

18 A. The elements would include a  
19 medication guide that went to the patient  
20 each and every time he or she picked up  
21 their prescription from the pharmacy.  
22 Education of healthcare providers on all  
23 of the elements that we've previously  
24 spoken about. And a educational program

1 with an attempt to enroll as many  
2 physicians as possible to take the  
3 educational program.

4 Q. And if you turn to Page 24.  
5 This is a set of educational materials  
6 that were prepared as part of the REMS?

7 A. Yes. Yes.

8 Q. And if you go back to, two  
9 pages, you see a letter there. Well, let  
10 me -- I'm sorry, not two pages.

11 A. I believe you're looking at  
12 Page 16.

13 Q. Yeah, 16. What's Page 16?

14 A. This is the letter to  
15 healthcare providers that would have been  
16 sent out as part of the REMS program.

17 Q. So they would have been sent  
18 out, at product launch, this entire  
19 package of educational materials?

20 A. Yes.

21 Q. Was Nucynta a successful  
22 product?

23 A. Success is relative. It was  
24 not as successful as we had hoped it

1 would be.

2 Q. And did you have a view on  
3 why that was?

4 A. We knew that we were  
5 introducing a new opioid into a  
6 marketplace with a lot of other options,  
7 including options that were available  
8 generically.

9 Q. And ultimately what happened  
10 to the Nucynta products at Janssen?

11 A. We divested the product and  
12 sold it to another company.

13 Q. And that occurred when?

14 A. In 2015.

15 Q. Just one last -- one last  
16 question.

17 In your testimony earlier,  
18 you were asked questions about the  
19 difficulty of doing a clinical trial with  
20 -- prospective clinical trial with an  
21 endpoint of addiction.

22 Can you elaborate on the  
23 reasons why such a trial would be so  
24 difficult to do?

1           A.       There are a variety of  
2 reasons why that would be the case, if  
3 you're talking about a controlled  
4 clinical trial where the endpoint was  
5 addiction.

6                   To begin with, as the -- you  
7 would have to define addiction such that  
8 it could be assessed in a proper clinical  
9 trial. You would estimate the point of  
10 addiction such that you would get a  
11 sample size. Because the adverse event  
12 of addiction is considered to be rare in  
13 properly monitored patients, a  
14 statistical assessment of the number of  
15 patients that you would need to do such a  
16 clinical trial would be rather large,  
17 perhaps in the range of 100,000 patients  
18 or more.

19                   Moreover from an ethical  
20 standpoint, you would be enrolling these  
21 patients with instructions to the  
22 treating physician to see these patients  
23 on a regular basis so that he or she  
24 would be properly monitoring the patient.

1 In all of the clinical trials, you would  
2 have regular assessments, and the regular  
3 assessments would include elements that  
4 we've spoken of earlier as indicators of  
5 behaviors that would indicate abuse,  
6 misuse and diversion.

7 And there, from an ethical  
8 standpoint would need to be an  
9 intervention at that time. And that  
10 intervention may even include  
11 discontinuing the drug.

12 So the likelihood that you  
13 would reach the endpoint of interest with  
14 a reasonable number of patients in a  
15 reasonable period of time would be  
16 exceedingly small.

17 MR. LIFLAND: No further  
18 questions.

19 We'll take a five-minute  
20 break.

21 THE VIDEOGRAPHER: Okay.  
22 The time is 6:35 p.m. Going off  
23 the record.

24 (Short break.)

1 THE VIDEOGRAPHER: We are  
2 back on the record. The time is  
3 6:45 p.m.

4 - - -  
5 EXAMINATION

6 - - -

7 BY MS. CONROY:

8 Q. Dr. Moskovitz, for probably  
9 about the last two hours or so you've  
10 testified about the Duragesic and the  
11 Nucynta label, the treatment of chronic  
12 pain with opioids, different  
13 formulations, the reservoir, the matrix,  
14 abuse, diversion, misuse, addiction,  
15 iatrogenic addiction, monitoring --  
16 monitoring programs, all of those things,  
17 right?

18 A. Yes.

19 Q. And you've been designated  
20 by Janssen as the person most  
21 knowledgeable about studies, trials,  
22 reports about opioids, including  
23 Duragesic, as well as the label and  
24 warnings and adverse events and the

1       benefits and the risks of Duragesic,  
2       Nucynta, and -- and opioids generally,  
3       would you agree?

4               A.       Yes.

5                       MR. LIFLAND: I object to  
6                       the form of the question. He's  
7                       not designated as the person most  
8                       knowledgeable. It's a 30(b)(6)  
9                       corporate rep deposition.

10       BY MS. CONROY:

11               Q.       You can answer.

12               A.       That's my understanding.

13               Q.       And you were appointed the  
14       head of the pain division in medical  
15       affairs and you held that position -- and  
16       I know it had some name changes -- for  
17       approximately 11 years, correct?

18               A.       Yes.

19               Q.       You are a medical doctor?

20               A.       Yes.

21               Q.       You have prescribed opioids?

22               A.       I have.

23               Q.       Janssen believed you were  
24       qualified to head the division, correct?

1                   A.       Yes.

2                   Q.       Would you say that you are  
3       an expert with respect to pain,  
4       addiction, abuse, diversion, the label,  
5       Duragesic, all of those items?

6                   MR. LIFLAND:   Object to the  
7       form of the question.

8                   THE WITNESS:   That's a broad  
9       set.   I would say I have expertise  
10      in clinical trial methodology.  
11      I'm well versed in the label of  
12      our products.

13                  I certainly gained extensive  
14      amount of knowledge over general  
15      principles of pain management.   I  
16      have an extensive information  
17      about the benefits and risks of  
18      our products, the  
19      pharmacokinetics, the -- the  
20      formulations.

21                  But in -- in terms of the  
22      level of expertise, I mean clearly  
23      there are other experts in pain  
24      management, but overall I'm well

1                   versed in our products.

2       BY MS. CONROY:

3                   Q.       And that would include pain  
4       and addiction?

5                   A.       That would include pain and,  
6       with -- with respect to our compounds,  
7       the concerns of adverse events that --  
8       that include the potential for abuse,  
9       misuse, diversion.

10                          I'm not an expert on  
11       treating addiction, but in the sense  
12       of -- of the potential for our drugs to  
13       have as adverse events abuse, misuse and  
14       diversion, yes.

15                   Q.       What about the adverse event  
16       of addiction?

17                   A.       The -- the knowledge that a  
18       potent opioid such as our compounds,  
19       Duragesic and Nucynta, have the capacity  
20       for addiction, abuse, misuse and  
21       diversion, yes.

22                          (Document marked for  
23       identification as Exhibit  
24       Janssen-Moskovitz-40.)

1 BY MS. CONROY:

2 Q. I'll show you Exhibit 40.

3 Exhibit 40 is a -- an e-mail  
4 thread in June of 2006. It is  
5 JAN-MS-00957863 through 864. And if you  
6 would turn the page to the second page  
7 which is the first e-mail. And it is an  
8 e-mail to you from Dawn  
9 Sanderson-Bongiovanni, do you see that?

10 A. Yes.

11 Q. On June 19, 2006. And  
12 she -- I -- I saw her name. She was one  
13 of the individuals that's in the  
14 benefit/risk management group and she  
15 signs or she is one of the signators to  
16 the progress report that's filed with the  
17 FDA, the risk management progress report?

18 A. I'd have to go back to the  
19 document but I'll certainly take your --  
20 your word for that.

21 Q. I won't make you take -- I  
22 can show it to you, but --

23 A. That's fine.

24 Q. Okay.

1 "Dear Bruce, it was so nice  
2 to meet you at the data flow meeting last  
3 week" -- "last Monday. Thank you for  
4 hosting a lovely dinner. I'm writing in  
5 regard to the comments received from the  
6 FDA in response to the Duragesic risk map  
7 proposal. The agency expressed concern  
8 about the risk of iatrogenic addiction  
9 with chronic use of Duragesic.  
10 Therefore, I'm in the process of  
11 reviewing potential cases of iatrogenic  
12 addiction that have been reported to the  
13 company."

14 Those would be cases  
15 reported through the adverse event  
16 reporting mechanism, correct?

17 A. Yes.

18 Q. "As part of my background  
19 research I've read multiple articles in  
20 the past week with conflicting estimates  
21 for the incidence of addiction in  
22 patients with chronic pain. The  
23 variation is probably due to inherent  
24 differences between the study

1 populations," in parentheses, (AIDS  
2 patients versus burn patients) and  
3 differences in monitoring parameters. I  
4 was wondering if you could possibly cite  
5 a 'landmark' article that reflects  
6 current medical thinking about the  
7 occurrence and etiology of addiction  
8 (induced by opioid therapy). Thank you  
9 for sharing your expertise on this  
10 subject."

11 Do you know Dawn  
12 Sanderson-Bongiovanni, do you know her  
13 face-to-face?

14 A. No, I don't.

15 Q. Okay. Do you know where she  
16 works? I mean do you know what office  
17 location she works in?

18 A. It -- it would have been in  
19 the Titusville office. That's how she  
20 signs her name.

21 Q. And that's not where you  
22 were located?

23 A. No, I was up in the --

24 Q. And then you respond to her

1     that same day, actually five minutes  
2     later, and you say, "Dawn, I cannot.  
3     Pain and addiction are not my specialty.  
4     However, I'm copying your request to Gary  
5     Vorsanger and David Hewitt in my group.  
6     Gary is an anesthesiologist by training.  
7     David is a neurologist specializing in  
8     pain medicine. Gary, David, kindly  
9     address Dawn's questions. Thanks."

10                     Do you see that?

11                     A.     Yes.

12                     Q.     And then both men do respond  
13     that same day. And you can -- and you  
14     can read it, but Dr. Hewitt says,  
15     "Unfortunately the evidence supporting  
16     the low abuse potential among patients  
17     receiving opioids for chronic pain is not  
18     based upon strong data. I've seen  
19     numbers that suggest the rate of  
20     addiction is similar to the population at  
21     large and no higher."

22                     And Dr. Vorsanger says,  
23     among other things, that he's skeptical  
24     of the low rates, that Margo, Margo

1 McCaffery who is referenced in an e-mail,  
2 cite, and others cite.

3 Had you had -- you had  
4 conversations, do you know, with  
5 Dr. Vorsanger or Dr. Hewitt about their  
6 belief about the incidence of iatrogenic  
7 addiction with chronic pain patients  
8 taking opioids for chronic pain?

9 A. In a general sense we were  
10 aware that the data would not be  
11 considered high quality data when there  
12 is a methodology that -- that reports on  
13 what would be considered high quality  
14 data, which would be a controlled  
15 clinical trial. So the -- the reports  
16 oftentimes didn't cite the criteria by  
17 which they would make that diagnosis, the  
18 patient population that they explored,  
19 whether this was prospective or  
20 retrospective. So there was  
21 the understanding that there are data out  
22 there, and those are the best data  
23 available to us, but it doesn't  
24 necessarily reflect a true incidence of

1 abuse, misuse and diversion with opioids.

2 Q. Do you believe it doesn't  
3 represent the true incidence because the  
4 true incidence is higher?

5 A. Because the true incidence  
6 can't be arrived at with the methodology  
7 used in the papers that explored that.

8 Q. But it appears to me, and  
9 we'll ask Dr. Vorsanger about this,  
10 and -- and potentially Dr. Hewitt, but it  
11 seems to me that they believed that those  
12 studies also under -- under represent?

13 MR. LIFLAND: Object to the  
14 form of the question.

15 THE WITNESS: That may be  
16 the case. That that -- being a  
17 potentially inaccurate estimate,  
18 it may underestimate the rate of  
19 abuse, misuse, and diversion. And  
20 particularly addiction and those  
21 reports of addiction.

22 BY MS. CONROY:

23 Q. Is there a reason why you  
24 cited -- well, let me ask you this. Are

1     you familiar with the Porter & Jick  
2     study?

3             A.     Yes.

4             Q.     And you've cited that in the  
5     past?

6             A.     As part of what was  
7     available at the time that -- some --  
8     some of the earlier reports around  
9     incidence of abuse, misuse and diversion.  
10    Abuse.

11            Q.     When you cited that --  
12    actually a letter to the editor, when you  
13    cited that --

14            A.     Right.

15            Q.     -- it was -- you cited it a  
16    few times that I saw the most, the latest  
17    cite was in 2007 in the risk management  
18    plan, you didn't qualify that study or --  
19    I guess it's not a study -- letter to the  
20    editor.

21                    You didn't qualify it in any  
22    way and say I'm not sure that this study  
23    was done correctly or that it accurately  
24    reflects the -- the situation today.

1       Isn't that true?

2               A.       I didn't --

3                       MR. LIFLAND:   Object to the  
4               form of the question.

5                       THE WITNESS:   I didn't  
6               qualify it in that respect.

7       BY MS. CONROY:

8               Q.       Why did you cite it?

9               A.       Because it was part of the  
10       body of information.   There were  
11       relatively few reports of rates of abuse  
12       with the use of opioids.   And this was  
13       certainly one of the earliest, one of the  
14       largest, went through a large number of  
15       patients, and it was recognized in the  
16       pain literature as one point of  
17       reference.

18              Q.       But you understand that was  
19       not about abuse, that was about addiction  
20       that letter?

21              A.       Yes.

22              Q.       And are you familiar with  
23       the details of that letter?

24              A.       I'd have to go back to the

1 letter.

2 Q. Do you understand that it  
3 was with -- only concerning patients in a  
4 hospital?

5 A. Yes, that's my -- yes,  
6 that's my understanding.

7 Q. And for a very short period  
8 of time?

9 A. Yes.

10 Q. And a very short follow-up  
11 as well?

12 A. I'd have to go back to the  
13 letter to see what the follow-up period  
14 was.

15 Q. Is there a reason why you  
16 didn't tell Ms. Sanderson-Bongiovanni  
17 about the Porter and Jick?

18 A. I -- I referred it to the  
19 two individuals in my group, the two  
20 physicians who reported to me who may  
21 have been able to provide better data  
22 sources to her.

23 Q. But you knew there weren't  
24 any other data sources.

1           A.       I knew what I knew, and they  
2       may have -- and they may have had a  
3       broader knowledge base than I did.

4           Q.       You just told me there were  
5       very few large scale studies. Did you  
6       think that one got by you?

7           MR. LIFLAND: Object to the  
8       form of the question.

9           THE WITNESS: I don't know.  
10       I don't recall all of the sources  
11       of information around addiction.

12       BY MS. CONROY:

13           Q.       But you do recall that there  
14       aren't many?

15           A.       I recall that there weren't  
16       many. And I recall that in instances  
17       where they were reported, they may not  
18       have reported what criteria they used to  
19       make the diagnosis of addiction or the  
20       patient population or the duration of  
21       therapy. So there were limitations in  
22       the reports.

23           Q.       The only one that you cited,  
24       however, in the risk management plan was

1 Porter and Jick, correct?

2 A. I'd have to go back to the  
3 risk management plan. But I'll --

4 MR. LIFLAND: Object to the  
5 form of the question.

6 BY MS. CONROY:

7 Q. Let me ask it this way. You  
8 can't recall any other study concerning  
9 addiction to chronic pain medication  
10 other than Porter and Jick as you sit  
11 here today?

12 A. There were other studies  
13 that looked at issues -- at addiction in  
14 a population that received opioids.

15 Q. Do you recall what the  
16 results were?

17 A. That the overall incidence  
18 of addiction was relatively low.

19 Q. If you take a look at  
20 Ms. Sanderson-Bongiovanni response. She  
21 says, "Well, one thing is obvious from  
22 these responses. Medical affairs is not  
23 in the process of addressing the FDA  
24 comments on the issues of iatrogenic

1 addiction, so we're not duplicating  
2 efforts and resources."

3 Did you have any  
4 conversation with her about whether or  
5 not you were in fact going to assist in  
6 addressing the FDA's comments on the  
7 issues of iatrogenic addiction?

8 A. Well, we looked at our  
9 database of adverse event reports and did  
10 an analysis of our database relative to  
11 iatrogenic addiction. But I was not on  
12 that final -- no, I don't know.

13 Q. Were you -- were you  
14 involved in her progress report to the  
15 FDA with respect to the issue of  
16 iatrogenic addiction?

17 A. I would have reviewed that.

18 Q. You provided the database  
19 results for that progress report,  
20 correct, the issue with the 103 patients  
21 believed to be addicted, an adverse event  
22 of addiction?

23 A. That would have come from  
24 the benefit-risk management group, from

1 the group that received the adverse  
2 events, not from medical affairs.

3 Q. Okay. So the -- so what if  
4 anything would you have been providing to  
5 Sanderson-Bongiovanni to assist in the  
6 process of addressing the FDA comments?

7 A. The report on iatrogenic  
8 addiction was relative to Duragesic. If  
9 I go back to her original question, it  
10 appears that she's asking a broader  
11 question about iatrogenic addiction, not  
12 specific to Duragesic.

13 Q. Well, she says, "I'm writing  
14 in regard to the comments received from  
15 FDA in response to the Duragesic risk map  
16 proposal. The agency expressed concern  
17 about the risk of iatrogenic addiction  
18 with chronic use of Duragesic."

19 That sounds pretty specific  
20 to me.

21 A. Right, but she continues,  
22 "As part of my background and research,  
23 I've read multiple articles with  
24 conflicting estimates for the incidence

1 of addiction in patients with chronic  
2 pain, and she cites specific groups.

3 So she's asking for a  
4 landmark article about the occurrence and  
5 etiology of addiction, not -- I read that  
6 as not specific to Duragesic. She wants  
7 a backgrounder on addiction.

8 Q. Right. And instead of  
9 telling her anything, you respond that  
10 pain and addiction aren't your specialty.

11 A. I respond that there are  
12 better sources for the articles that she  
13 was looking for.

14 Q. And the two individuals who  
15 provided that source tell her that  
16 they're skeptical about the low rates of  
17 iatrogenic addiction, correct?

18 A. Correct.

19 Q. And yet she continues in  
20 that progress report that was marked as  
21 an exhibit at this deposition in --  
22 continuing to imply that the rates of  
23 iatrogenic addiction are low.

24 A. Because the available data

1     which could be questioned as to the  
2     patient population that they looked at,  
3     the criteria that they use to make that  
4     diagnosis, could be questioned. It was  
5     clear that the available data did not  
6     come from a controlled clinical trial.  
7     And so it had the limitations that we  
8     understood for retrospective databases or  
9     anything other than a controlled clinical  
10    trial.

11                   But it was -- we were trying  
12    to find the best available data at the  
13    time.

14           Q.     But you understand -- and  
15    I'm sure you have seen studies, that  
16    adverse event reporting picks up about 10  
17    percent, it's believed, of adverse events  
18    that are experienced by patients, because  
19    it's dependent upon doctors, and  
20    potentially others, reporting those  
21    adverse events, correct?

22           A.     I won't cite a rate. But  
23    yes, it's generally understood that the  
24    rate of reporting of adverse event is far

1 less than the actual incidence of adverse  
2 events. Yes, that was -- that was widely  
3 understood for almost all adverse events.

4 Q. However, that's not cited in  
5 the report to the FDA, correct?

6 A. No. But in the report to  
7 the FDA about iatrogenic addiction, we  
8 specifically state these are the cases we  
9 received.

10 Q. But you don't state that  
11 it's well known that adverse event  
12 reporting is a very inaccurate way of  
13 determining the true extent of adverse  
14 events?

15 A. We are reporting this to the  
16 Food and Drug Administration. And I  
17 think they, above all, would understand  
18 that there are limitations, significant  
19 limitations in rates of adverse event  
20 reporting that come into the company or  
21 to the FDA.

22 Q. Do you think when you cite  
23 Porter and Jick to them, they likewise  
24 understand the limitations of that letter

1 to the editor?

2 A. I do think that the FDA  
3 understands the limitations of any source  
4 of data, and they can compare those  
5 sources of data with respect to the  
6 accuracy. So clearly a randomized  
7 controlled clinical trial is going to  
8 give you more accurate data than an  
9 observational study or than a study in  
10 which there were reports of that come  
11 into a company. I'm clear that the FDA  
12 understands the limitations of those  
13 data.

14 Q. You also spoke during your  
15 direct examination about animal models  
16 and that there were some -- you talked  
17 about some dual mechanisms of action with  
18 the mu receptors in animal models and  
19 animal trials. Do you recall that  
20 testimony?

21 A. Yes.

22 Q. Are you familiar with the  
23 reference in your risk management plan to  
24 an animal study that talked about low

1 doses after one or more months of  
2 treatment that animals can develop opioid  
3 addiction?

4 A. I'd have to look at the  
5 document. I don't recall it offhand.

6 Q. Let's take a look at it. I  
7 don't --

8 MS. CONROY: Mr. Lifland,  
9 maybe you can help him find the --  
10 I don't have the exhibit number.  
11 It's about that thick. It's an  
12 exhibit right there. And it is  
13 the risk management plan from  
14 June 14, 2007. I have a -- I can  
15 pass you a copy if you want to see  
16 it.

17 MR. LIFLAND: This?

18 MS. CONROY: Except -- I  
19 can't see it.

20 MR. LIFLAND: The plan or  
21 the report?

22 MS. CONROY: The plan.  
23 That's it right there. Do you  
24 have the exhibit number?

1 MR. LIFLAND: 29.

2 MS. CONROY: 29. Great.

3 Thank you.

4 BY MS. CONROY:

5 Q. If you go to Page 29.

6 A. I'm not there yet.

7 Q. Oh, here. Let me give you  
8 this one. It will be faster. If you go  
9 to Page 29. I gave my clean copy away,  
10 but I'll put it on the screen. Hide my  
11 notes.

12 "At low doses after one or  
13 more months of treatment, animals can  
14 develop opioid addiction."

15 Do you see that?

16 A. I do.

17 Q. Do you know what -- that  
18 study is not cited here. Do you know  
19 what it is?

20 A. My assumption is that, as  
21 part of development of any program, we  
22 would be looking at preclinical data and  
23 animal data, and that this was one of the  
24 studies that helped to assess the

1 potential for addiction in -- it was a  
2 study that was done in an animal model.  
3 But we knew that fentanyl, by virtue of  
4 being a Schedule II compound, had a high  
5 potential for abuse, misuse and  
6 addiction.

7 Q. Well, animals aren't  
8 misusing or abusing it, correct?

9 A. No. Correct.

10 Q. So this would be a study  
11 about addiction?

12 A. In -- yes.

13 Q. Will I find this study in  
14 the -- I have lots of references that I  
15 got at your 30(b)(6) deposition. Will  
16 this study be part of the NDA, do you  
17 think, or?

18 A. I would imagine it would be  
19 part of the NDA.

20 Q. Okay. You don't have any  
21 specific memory of what this is?

22 A. I don't. But again we  
23 understood all potent opioids have  
24 addictive properties and, if administered

1 to laboratory animals, you can --  
2 chronically administering it can lead to  
3 addiction.

4 Q. And oftentimes animal --  
5 animal models are used to give some  
6 insight into what might happen with  
7 humans, correct? That's the reason that  
8 you do animal model studies, right?

9 A. Certainly insight into  
10 scheduling a product, and insight into  
11 potential risks for the product.

12 Q. One month of treatment with  
13 a controlled substance, an opioid or  
14 something like a fentanyl patch, that  
15 would be fairly typical for chronic pain  
16 patients, correct?

17 A. One month would be typical  
18 for chronic -- for treating chronic pain  
19 moderate -- severe enough, if they met  
20 the criteria with a Duragesic -- with a  
21 Duragesic patch, yes.

22 But I don't want to indicate  
23 that you can directly translate animal  
24 models into a human model. We know that

1     opioids are addictive, therefore, they  
2     need to be properly prescribed with the  
3     appropriate monitoring around them and  
4     the appropriate instruction to patients  
5     and assessing patients.

6             Q.     Correct.

7                     I know you testified earlier  
8     that RADARS is independent of Janssen,  
9     correct?

10            A.     Yes.

11            Q.     Do you know if RADARS is  
12     independent of any other pharmaceutical  
13     company?

14            A.     It is.

15            Q.     It's a standalone?

16            A.     It's a standalone.

17            Q.     Do you know if Janssen has  
18     or had a licensing agreement with Sandoz  
19     to either manufacture or market generic  
20     Duragesic?

21            A.     It's my understanding that  
22     we had an agreement with Sandoz to market  
23     an authorized generic of Duragesic.

24            Q.     And was it -- that was in

1 writing, I assume?

2 A. I'm sure it was. I never  
3 saw the contract.

4 Q. Okay. And while you were  
5 employed at Janssen, do you know if  
6 Janssen or Johnson & Johnson, or Janssen  
7 Ortho-McNeil ever owned a company called  
8 Noramco that -- that manufactured opiates  
9 or the raw material that potentially was  
10 used for any Janssen opioid products?

11 A. I was aware of a company  
12 Noramco. I don't recall the exact  
13 relationship, whether it was part of the  
14 Johnson & Johnson organization, but I  
15 knew that, that they manufactured raw  
16 materials.

17 Q. Do you know if they  
18 manufactured raw materials for other  
19 pharmaceutical companies' products?

20 A. I don't know.

21 Q. Who would know that?

22 MR. LIFLAND: Object to the  
23 form of the question.

24 THE WITNESS: Probably

1                   somebody in the supply chain.

2       BY MS. CONROY:

3                   Q.       Do you know if -- or had you  
4       ever heard that they manufactured the  
5       opiate for OxyContin?

6                   A.       I don't know.

7                   Q.       You were -- Exhibit 33 was  
8       marked during your direct testimony.

9                             What I'm going to mark is a  
10       cover letter for that paper, I mean  
11       for -- for your report.

12                   A.       So I don't need to find  
13       it --

14                   Q.       No, I'm going to give you  
15       the whole thing even though it will kind  
16       of be an extra.

17                             The -- I will tell you that  
18       the attached is already marked as  
19       Exhibit 33.

20                             (Document marked for  
21       identification as Exhibit  
22       Janssen-Moskovitz-41.)

23       BY MS. CONROY:

24                   Q.       So this is 41, and this is

1 33.

2 Exhibit 41 is an e-mail from  
3 you to Ravi Desiraju and Michael Kaufman  
4 with cc's to Lisbeth Warren, Gary  
5 Vorsanger and Jean Farrell. And it's  
6 dated April 28 of 2008.

7 And in this e-mail you  
8 attach your summary of the RADARS report  
9 on rates of abuse and diversion for  
10 transdermal fentanyl products. And you  
11 say, "I understand. We will not provide  
12 this assessment with the RADARS report we  
13 submit to the FDA."

14 Do you see that?

15 A. Yes.

16 Q. So Exhibit 33, which we've  
17 already looked at, would not be submitted  
18 to the FDA, correct?

19 A. Correct.

20 Q. "In that case, it becomes an  
21 internal document justifying our move to  
22 a clinical development plan for a switch  
23 from the reservoir to the matrix  
24 transdermal patch, would anyone need to

1 review it."

2 Do you see that?

3 A. Yes.

4 Q. And is it still your  
5 understanding that this remained an  
6 internal Janssen document to justify the  
7 clinical development plan to move from  
8 reservoir to matrix?

9 A. I believe so. I mean, our  
10 commitment to the FDA was that before any  
11 decision to move from a reservoir patch  
12 to the matrix patch, we would want to  
13 review the available RADARS data to  
14 satisfy ourselves that the concerns we  
15 expressed in 2001 and 2004 over potential  
16 differences between the two formulations  
17 were not coming to fruition and that once  
18 we had the data for our own use, we were  
19 comfortable that it, in fact, did not  
20 show an increased rate of abuse, misuse  
21 and diversion. And so we felt  
22 comfortable with the decision to move to  
23 the matrix patch which was what the FDA  
24 had preferred we do.

1 I don't know whether the  
2 final decision was to submit those data  
3 or simply acknowledge to the FDA that  
4 yes, we've had an opportunity to review  
5 the data, we're comfortable that the  
6 concerns we expressed in 2001 and 2004  
7 were allayed and that we will move  
8 towards the development of a matrix.

9 Q. And -- and you wrote that  
10 out in Exhibit 33. But if you take a  
11 look at the second page of Exhibit 33,  
12 you go -- you continue to say, "While  
13 concerns remain that in the future rates  
14 of abuse and diversion may increase,  
15 because the matrix formulation can be cut  
16 and diverted in ways the reservoir  
17 cannot. A matrix formulation has  
18 advantages over a reservoir formulation  
19 in that it cannot 'leak' if a  
20 manufacturing defect leads to an unsealed  
21 reservoir."

22 Do you see that?

23 A. Yes.

24 Q. So you still had concerns

1 about the abuse and diversion of the  
2 matrix patch or the matrix technology?

3 A. We're always concerned about  
4 ways in which any of our products might  
5 be abused, misused and diverted. At this  
6 point in time we had -- we had no  
7 evidence that over the previous few  
8 years, that the rates differed between  
9 the two formulations.

10 We were certainly going to  
11 continue our surveillance program so if  
12 we started to see increases in rates  
13 of -- of cutting the patch and diversion  
14 of the patch, based upon what we've  
15 already discussed as outcomes of our  
16 surveillance program, we might have taken  
17 additional steps to minimize those risks.

18 Q. But as of -- as of the date  
19 that you were internally justifying this  
20 switch, and the date on this is April  
21 of -- end of April of 2008, you -- you  
22 still had concerns that there would be an  
23 increase in abuse and diversion with the  
24 matrix?

1           A.       We knew that there were ways  
2       in which the matrix patch could be  
3       abused, misused and diverted that  
4       differed from the Duragesic reservoir  
5       patch. I don't think those concerns  
6       would ever completely dissipate. But  
7       that's why we monitor.

8           Q.       Okay. And so if we go back  
9       to what was said in the Mudskipper report  
10      from 2004, which was Exhibit 25, that  
11      "the availability of a fentanyl matrix  
12      patch is likely to increase the diversion  
13      of patches with major public health  
14      consequences," and then it goes onto the  
15      two bullet points of -- of further  
16      explaining that, that's really the same  
17      thing that you're saying in the internal  
18      justification memo, correct?

19                   MR. LIFLAND: Object to the  
20                   form of the question.

21      BY MS. CONROY:

22           Q.       -- that you were  
23      concerned that -- you were concerned that  
24      diversion and abuse might increase with

1 the matrix patch?

2 MR. LIFLAND: Object to the  
3 form of the question.

4 THE WITNESS: At the time of  
5 the 2004 report, this was a  
6 hypothetical, because there was no  
7 matrix patch on the market in the  
8 U.S.

9 And so we did the studies  
10 that informed our concerns about  
11 risks of -- differential risks of  
12 abuse, misuse and diversion.

13 In 2007, 2008 we had  
14 available data from the RADARS  
15 reports that informed us that the  
16 differences were not the degree  
17 that we had perhaps anticipated in  
18 2004, and so we felt comfortable  
19 with the decision to switch from a  
20 reservoir to a matrix.

21 The concerns about the ways  
22 in which a drug might be abused,  
23 misused and diverted would remain.  
24 And that's why we continue our

1 surveillance programs.

2 BY MS. CONROY:

3 Q. Right. Because the  
4 availability of a fentanyl matrix patch  
5 is likely to increase the diversion of  
6 patches with major public health  
7 consequences, has never changed, correct?

8 MR. LIFLAND: Object to the  
9 form of the question.

10 THE WITNESS: That -- that  
11 was our -- lacking any actual use  
12 data, this was our assessment in  
13 2004 based upon the data that we  
14 generated in the course of 2003,  
15 2004.

16 By 2007, 2008, we had actual  
17 use data. That allayed the  
18 concern at the time and helped us  
19 make the decision that we would  
20 follow the FDA's preference for  
21 moving from a Duragesic reservoir  
22 patch to a matrix patch, which we  
23 identified as having certain  
24 advantages over a reservoir patch.

1 BY MS. CONROY:

2 Q. I accept all of that. But  
3 you still remained concerned about an  
4 increase in diversion with a matrix  
5 patch. You had that concern in 2004.  
6 You had that concern in 2008. And it  
7 sounds like you have that concern today.

8 MR. LIFLAND: Object to the  
9 form of the question.

10 THE WITNESS: We're always  
11 aware of ways in which our drugs  
12 might be abused, misused and  
13 diverted. We're always -- we're  
14 always aware that there are  
15 differences in the ways a  
16 reservoir patch and a matrix patch  
17 might be abused, misused, and  
18 diverted. We had greater concerns  
19 before we had real world data.

20 By 2007, 2008, there were  
21 enough data that allayed those  
22 concerns.

23 Why that was the case,  
24 that's hypothetical. It may be

1           because there is more attraction  
2           to other compounds that are on the  
3           market.

4                     It doesn't change the fact  
5           that there are ways in which a  
6           matrix Duragesic patch can be  
7           abused that differ from the  
8           reservoir patch. We continued our  
9           surveillance programs to see if at  
10          any point that would be the case.

11                    In theory, if you took all  
12          other Schedule II products off the  
13          market and the only drugs that  
14          were available were a reservoir  
15          patch and a matrix patch, there  
16          would be more abuse, misuse and  
17          diversion of a matrix patch  
18          because, in some ways, it was  
19          easier.

20       BY MS. CONROY:

21                Q.       I understand what you're  
22       saying. My question is not about the  
23       relationship between a reservoir patch  
24       and matrix patch. It's strictly that

1     once you made the decision with respect  
2     to the matrix patch to go with the matrix  
3     patch, you still had concerns about abuse  
4     and diversion?

5                     MR. LIFLAND: Object to the  
6                     form of the question.

7                     THE WITNESS: We always had  
8                     concerns about abuse, misuse and  
9                     diversion of our Duragesic  
10                    product, whether it was reservoir  
11                    or matrix. That's why we  
12                    monitored for signals of abuse,  
13                    misuse, and diversion. We're  
14                    simply aware that there were  
15                    different ways that you could  
16                    abuse, misuse and divert a matrix  
17                    patch. We always had concerns for  
18                    both of the formulations that they  
19                    could be abused, misused and  
20                    diverted.

21     BY MS. CONROY:

22                    Q.     And those concerns existed  
23                    in 2004 and they remained a concern for  
24                    the matrix patch in 2008.

1           A.       And that's why --

2                   MR. LIFLAND:   Object to the  
3           form of the question.

4                   THE WITNESS:   And that's why  
5           we continued our surveillance  
6           programs.   Yes, we continued to  
7           have concerns about ways in which  
8           our products could be abused,  
9           misused and diverted.

10       BY MS. CONROY:

11               Q.       You testified right at the  
12       beginning of your direct testimony about  
13       addiction -- definitions of addiction and  
14       dependence.   Do you remember saying that?

15               A.       I do.

16               Q.       You were not suggesting that  
17       Janssen scientists and researchers and  
18       doctors and sales reps are free to use  
19       any definition they want when they are  
20       referring to either addiction or  
21       dependence or abuse or misuse or  
22       anything?

23               A.       I believe my testimony was  
24       that there was no company-wide definition

1 of these terms that was understood by  
2 everyone who used these terms.

3 Q. Was there a medical  
4 affairs-wide definition of those terms --

5 A. No.

6 Q. -- or some of those terms?

7 A. No.

8 Q. Are there -- I do see that  
9 in certain pieces, for example the  
10 Exhibit 30 -- you don't need to really  
11 pull it out, I don't think. But this is  
12 one of the -- this is -- this is one of  
13 the REMS from -- it must be later if it's  
14 a REMS, right?

15 A. Yes.

16 Q. Yeah. The -- there are  
17 definitions listed at the beginning of  
18 the document, correct? But that's good  
19 scientific practice, right, if you're  
20 writing, and you're going to be using  
21 particular terms, to define those terms  
22 somewhere in the document?

23 A. Yes.

24 Q. Was it the practice in

1 medical affairs to define terms that at  
2 least medical affairs was using in their  
3 documentation?

4 A. That would depend upon the  
5 context. If we were doing a clinical  
6 trial where we had to define a term or  
7 how we would arrive at that diagnosis,  
8 then it would be defined in the clinical  
9 trial.

10 In general use, we would use  
11 the terms that were widely identified and  
12 defined by well-recognized societies that  
13 managed -- that did pain management. The  
14 American Academy of Pain Management has  
15 definition of these terms. The American  
16 Pain Society has a definition of these  
17 terms. There are DSM-IV definitions of  
18 these terms.

19 Q. You would agree with me that  
20 that would be good scientific practice  
21 for a pharmaceutical company to use a  
22 common definition when -- I'm not talking  
23 about clinical trials where you are  
24 laying it out. I'm not talking about

1 analyses of prior literature by other  
2 authors. I'm talking about studies,  
3 reports, writings by the medical affairs  
4 department at Janssen, it would be good  
5 scientific medical practice to have a  
6 common definition, correct?

7 MR. LIFLAND: Object to the  
8 form of the question.

9 THE WITNESS: It would  
10 depend on the context. So if we  
11 were talking about adverse event  
12 reports, it may simply be the way  
13 it was defined by the reporter.  
14 If we are talking about internal  
15 documents, it would probably be  
16 the understanding of these terms  
17 as used by the medical societies,  
18 the broadly accepted use of these  
19 terms.

20 That doesn't necessarily  
21 mean that an individual who used  
22 the terms outside of a document  
23 like a risk management document  
24 would be using the terms in the

1 same manner that a group where the  
2 terminology is reviewed by a large  
3 number of individuals would use  
4 it.

5 BY MS. CONROY:

6 Q. So if I'm reading Janssen  
7 documents over a period of time, I need  
8 to be aware that the definition of  
9 addiction, dependence, abuse, misuse, may  
10 change with respect to the context it's  
11 used?

12 A. And who is writing the  
13 report and the level of expertise that he  
14 or she has.

15 Q. You were shown Exhibit 34,  
16 which was one of your key opinion leaders  
17 and Dr. Passik and several Janssen  
18 employees that have a brief report on  
19 tools to assess and document pain  
20 outcomes in chronic pain patients  
21 receiving opioid therapy. Do you recall  
22 that?

23 A. You're referring to the  
24 PADT, yes.

1           Q.     I'm going to put that on  
2     there.   PADT.   This study has the PADT  
3     inside the study, and I know we saw a  
4     color version of the PADT as well,  
5     correct?

6           A.     Yes.

7           Q.     But this -- this is offered  
8     as a tool by Dr. Passik and others.   But  
9     it was -- it hadn't been tested, right?  
10    It could prove helpful in clinical  
11    management?

12          A.     It hadn't been validated.  
13    But we -- in the development of the tool  
14    we used -- I think it describes how the  
15    tool was developed in the paper.

16          Q.     Right.   We had predictive  
17    validity through longitudinal use of the  
18    tool.   But you said that must be  
19    confirmed.

20          A.     Confirmed.

21          Q.     So it had not yet been  
22    confirmed at the time this article was  
23    written, correct?

24          A.     That's correct.

1           Q.     And studies are needed to  
2     clarify the interval of assessment that  
3     optimally balances the need to minimize  
4     clinician burden with the need to validly  
5     assess and document outcomes that may  
6     change continually over time, correct?

7           A.     Yes.

8           Q.     And so while this was a tool  
9     that was offered to physicians, we have  
10    no evidence as of today that this tool --  
11    that anyone is using it or that it works?

12          A.     I don't know the level to  
13    which they are using it. Certainly it  
14    was part of the recommendations of NIDA,  
15    as we spoke about. But I don't know the  
16    numbers.

17                   As a tool for documentation,  
18    which is to say if someone went to a  
19    physician and asked him or her, "On what  
20    basis did you choose," they could at --  
21    at least pull this tool up, if they were  
22    using it to say, "Okay, here was my  
23    assessment of the patient at the time  
24    that I saw the patient."

1           Q.     Sure. And it might be great  
2     for that. But we have no idea who is  
3     using it and for how long they use it and  
4     whether it actually works, even if people  
5     are using it.

6           A.     It works as a tool to  
7     document the decision, yes, it -- it  
8     would be a valuable tool to document  
9     their decision.

10                   Whether, by doing so and the  
11     frequency with which you're doing it  
12     leads to a lower risk for behaviors that  
13     predict abuse, misuse and diversion,  
14     that's part of the validation. We don't  
15     know that.

16           Q.     Right. And that's also true  
17     of addiction, correct, it's not just  
18     abuse, misuse and diversion, it's  
19     addiction as well?

20           A.     That's correct.

21           Q.     And earlier you were  
22     discussing the -- why doing a study with  
23     addiction as a primary endpoint would be  
24     impractical. Do you recall that

1 testimony?

2 A. Yes.

3 Q. And when you were discussing  
4 the reasons why it would be impractical,  
5 that's really the reason why it's  
6 difficult for even a treating physician  
7 to understand what's happening with a  
8 patient who has chronic pain, is being  
9 prescribed opioid therapy and may or may  
10 not be exhibiting aberrant behavior,  
11 correct?

12 MR. LIFLAND: Object to the  
13 form of the question.

14 THE WITNESS: I'm not sure  
15 of the -- that the conclusion we  
16 have about use of a clinical trial  
17 pertains to assessment of an  
18 individual patient sitting in  
19 front of a treating physician.

20 The individual patient  
21 sitting in front of a treating  
22 physician, that treating physician  
23 should assess that individual for  
24 behaviors that might be suggestive

1 of the potential for addiction or  
2 actual addiction and make a  
3 decision for that patient what the  
4 further method of care should be.

5 That's different than a  
6 clinical trial. I wouldn't equate  
7 the two.

8 BY MS. CONROY:

9 Q. What I understood you to say  
10 was when a physician in a clinical trial  
11 was presented with that problem, very  
12 often they wouldn't see the patient  
13 anymore, the patient would be gone. I  
14 think you don't actually -- there would  
15 be a discontinuance of the drug or there  
16 wouldn't be an ability to follow up with  
17 that patient.

18 A. I said that that was one of  
19 the concerns we would have in such a  
20 clinical trial, that you -- that there  
21 would be a high dropout rate among  
22 patients such that you might not even be  
23 able to get to an endpoint of -- an  
24 accurate endpoint of addiction.

1                   What I didn't mention  
2   earlier too is the best you can do in  
3   such a clinical trial would be to get,  
4   perhaps, a rate of iatrogenic addiction.  
5   You certainly wouldn't be looking at  
6   addiction in a subject population that  
7   was outside of the specific patient who  
8   gave informed consent to be in that  
9   trial.

10                Q.     Of course, right. My point  
11   was that that real world situation,  
12   either in the clinical trial or in the  
13   real world, is what makes it difficult,  
14   because when patients are suspected of  
15   having aberrant behavior, very often the  
16   physician stops prescribing the opioid,  
17   correct?

18                A.     Well, that's one  
19   possibility. But another possibility  
20   would be, as I spoke about earlier,  
21   closer monitoring of the patient,  
22   instituting other elements of monitoring,  
23   opioid agreements, urine monitoring, or  
24   referring that patient to a pain

1 specialist who has greater expertise in  
2 monitoring patients with higher risk of  
3 abuse, misuse and addiction.

4 Q. And I know you talked about  
5 the label and the monitoring of  
6 addiction.

7 Do you have any evidence  
8 that signing contracts or urine testing  
9 or any of those things actually work to  
10 reduce the incidence of addiction or  
11 abuse or misuse?

12 A. I don't. And in fact, it's  
13 my understanding that it's unclear at  
14 this point whether those elements of  
15 intervention do so.

16 Q. So while the label says  
17 monitor your patient, isn't it fair to  
18 say it's not entirely clear what the  
19 components of monitoring a patient that  
20 is exhibiting some signs of aberrant  
21 behavior really means?

22 A. The level of evidence over  
23 what those interventions would lead to is  
24 not at a high level of accuracy.

1           Q.     You also testified that a  
2     controlled dose is a benefit of  
3     Duragesic. Do you recall that? You were  
4     looking at the label at the time when you  
5     were talking about.

6           A.     I do.

7           Q.     And you said it was because  
8     there are lower high concentrations as  
9     the drug is entering the bloodstream and  
10    you don't go as low as an orally  
11    administered drug as it wears off. Do  
12    you recall that?

13          A.     I do. That there was a more  
14    consistent delivery of a concentration of  
15    fentanyl over the 72-hour period.

16          Q.     So in effect, lower highs  
17    and higher lows for a Duragesic patch?

18          A.     That would be one way of  
19    putting it.

20          Q.     Is that -- is that actually  
21    in the label, that benefit?

22          A.     Not as a benefit. We  
23    present the pharmacokinetic data.

24          Q.     And the pharmacokinetic data

1 shows the lower highs and the higher  
2 lows?

3 A. That you would maintain a  
4 consistent level of fentanyl over that  
5 72-hour period.

6 Q. And is that in normal human  
7 volunteers?

8 A. Yes.

9 Q. And do you know for how long  
10 those tests were conducted?

11 A. I believe in the package  
12 insert it's over two -- two, 72-hour  
13 periods.

14 Q. So about -- about -- a  
15 little under three weeks?

16 A. Once they achieved steady  
17 state, then there was -- there were two,  
18 72-hour periods after that.

19 Q. Do you know if that's ever  
20 been tested in chronic pain patients for  
21 longer than three or four weeks?

22 A. I'm sorry, I don't want  
23 to -- if what has been tested?

24 Q. The -- the serum blood

1 levels, whether or not the concentration  
2 was -- the highs were lower, and the lows  
3 were higher?

4 A. So the principles of  
5 pharmacokinetics inform the -- the  
6 clinical -- the trial that was done that  
7 looked at the pharmacokinetics, it was  
8 understood based upon principles of  
9 pharmacokinetics, that once you reach a  
10 steady state, that you could predict the  
11 longer term concentrations based upon  
12 those steady-state concentrations of  
13 fentanyl beyond the period of time in  
14 which you are measuring it.

15 Q. Do you know if that  
16 specifically has been tested with respect  
17 to fentanyl or some other opioid, or is  
18 that just a principle of pharmacokinetics  
19 that, regardless of the drug, once you  
20 reach steady state, it would remain that  
21 way?

22 A. That's a general principle  
23 of pharmacokinetics, that once you reach  
24 a steady state, a constant dosing, at

1     whatever interval, because you're --  
2     you're dosing at that interval to reach  
3     the steady state. But by definition, the  
4     steady state would indicate that the  
5     doses after that point would give you  
6     peak concentrations within a certain  
7     range and trough low concentrations  
8     within a certain range. That's a  
9     generally known principle of  
10    pharmacokinetics.

11           Q.     Do you know whether or not  
12    there were any specific tests of  
13    Duragesic over -- that -- that lasted for  
14    longer than the tests that are here in  
15    the label that went for, I'm not entirely  
16    sure, maybe 19 days after steady state  
17    was achieved?

18           A.     There were additional  
19    pharmacokinetic studies, certainly the  
20    pharmacokinetic studies that looked at  
21    heat. We did pharmacokinetic studies  
22    with the bio occlusive overlay. We did  
23    pharmacokinetic studies that looked at  
24    bioequivalence when we changed

1 formulations. I don't recall that any  
2 extended beyond the period of time that  
3 you're seeing in the label or that gave  
4 different information which then the FDA  
5 might have included in the label.

6 Q. We already covered this one.

7 MS. CONROY: So I'm done.

8 MR. LIFLAND: I have just a  
9 couple of follow-ups.

10 MS. CONROY: Do you want to  
11 do it from there or do you want to  
12 come across?

13 MR. LIFLAND: I think I will  
14 do it from there.

15 THE VIDEOGRAPHER: All  
16 right. Remove your microphones.  
17 The time is 7:42 p.m. Off the  
18 record.

19 (Short break.)

20 THE VIDEOGRAPHER: The time  
21 is 7:44 p.m. Back on the record.

22 - - -

23 EXAMINATION

24 - - -

1 BY MR. LIFLAND:

2 Q. Dr. Moskovitz, just a couple  
3 of follow-up questions.

4 First, relating to  
5 Exhibit 41. Do you have that?

6 A. I do. It's the top  
7 document.

8 Q. This is the document that  
9 indicates that the company was treating  
10 its assessment for going forward with the  
11 development program for the matrix  
12 patches that the FDA wanted as an  
13 internal company document. There's no  
14 suggestion in here though that the  
15 company did not send the RADARS data  
16 itself to the FDA?

17 MS. CONROY: Objection.

18 THE WITNESS: That's  
19 correct. That's correct. We sent  
20 the RADARS data as part of our  
21 obligation for the risk management  
22 program.

23 BY MR. LIFLAND:

24 Q. And in fact, it says here,

1 "The RADARS report we submit to the FDA,"  
2 indicating the data is sent, correct?

3 A. Yes.

4 Q. Let's go to Exhibit 29.

5 A. 29. I've got it.

6 Q. Can you turn to Page 39.

7 A. I have it.

8 Q. You'll see there's a  
9 statement on Page 39, mostly down the  
10 third paragraph that says, "For example,  
11 in a retrospective review of over 12,000  
12 hospital patients, only four potential  
13 addicts were identified."

14 And there are some  
15 footnotes.

16 You understand that that --  
17 at least one of those citations is a  
18 reference to the Porter and Jick survey?

19 A. It's my understanding that  
20 we cited it. I can't say it's 14 or 15.

21 Q. We can confirm that --

22 A. Actually, I have it here.

23 15 is the Porter and Jick, yes.

24 Q. And in fact, the

1 representation of that is accurate,  
2 correct, it tells -- it cites it as a  
3 survey of hospital patients, correct?

4 A. Yes.

5 Q. So it tells the reader that  
6 it's a hospital setting, correct?

7 A. Yes.

8 MS. CONROY: Objection.

9 BY MR. LIFLAND:

10 Q. It tells the reader that  
11 it's survey data, correct?

12 A. A retrospective review would  
13 be survey data, yes.

14 Q. And it indicates there have  
15 been no large prospective studies of  
16 iatrogenic drug addiction, correct?

17 A. Yes.

18 Q. So nothing is being  
19 inaccurately represented here, correct?

20 A. Yes.

21 Q. Now, in fact what's being  
22 represented is that we don't have much  
23 data, correct?

24 A. Yes.

1           Q.       And is that the reason why  
2       the company continues to track these  
3       adverse events as best it can?

4           A.       Yes. We knew that there  
5       were inadequate data on the true  
6       incidence of any of these terms. And  
7       so -- especially specifically with  
8       Duragesic, because all of these data were  
9       developed on all opioid compounds. And  
10      so that's why we continued to maintain a  
11      surveillance program for our compounds.

12          Q.       And in all the years, in all  
13      these surveys with the risk management  
14      plan, did you see evidence of high  
15      addiction problems with Duragesic as  
16      compared to other opioid analgesics?

17          A.       I'm certainly glad you  
18      qualified that with "as compared to other  
19      opioid analgesic products."

20                   In all streams of  
21      surveillance that we received, rates of  
22      abuse and diversion were consistently low  
23      risk or very low for Duragesic relative  
24      to other extended-release opioid

1 compounds.

2 And non extended-release.

3 Certainly hydrocodone was included in  
4 those surveillance studies.

5 Q. And let me show you  
6 exhibit --

7 MR. LIFLAND: Did we mark --  
8 did we mark the iatrogenic  
9 addiction report that I showed  
10 him?

11 MS. CONROY: I thought you  
12 had.

13 MR. RODRIGUEZ: I thought  
14 you did.

15 THE WITNESS: I thought you  
16 did too.

17 Here we go. It's  
18 Exhibit 37.

19 MS. CONROY: This is part of  
20 your pile. It's in there.

21 BY MR. LIFLAND:

22 Q. Take a look at Exhibit 37.  
23 This is the review of the adverse event  
24 reports of addiction for Duragesic,

1 correct?

2 A. The adverse events reported  
3 to our safety group with the term  
4 "addiction," yes.

5 Q. And it goes into some  
6 detail. It has exactly how they analyzed  
7 and searched and figured out which ones  
8 they could characterize as reports of  
9 addiction based on what they were  
10 attempting to look at, correct?

11 A. Yes.

12 Q. And the report is very clear  
13 that what they are looking at is not  
14 anything other than reports that are  
15 received in an adverse event database,  
16 correct?

17 A. Correct.

18 Q. And in fact, in the  
19 conclusion, when you read the  
20 conclusion --

21 MS. CONROY: What page is  
22 that on?

23 MR. LIFLAND: On 16. Well,  
24 it's shortly before the

1 conclusion.

2 THE WITNESS: It's part of  
3 the discussion.

4 BY MR. LIFLAND:

5 Q. Right. It's the discussion.  
6 It indicates that, "The reporting rate  
7 must be considered very rare given that  
8 there are 103 cases over 1.6 billion  
9 patient days."

10 You'd agree with that,  
11 right?

12 A. Yes.

13 Q. And you'd agree that it  
14 would be also very rare even if you  
15 assumed that 90 percent of the cases  
16 weren't reported, correct? If it was a  
17 thousand over 1.6 billion patient days,  
18 that would be a low reporting rate?

19 A. It would still be --

20 MS. CONROY: Objection.

21 THE WITNESS: It would still  
22 be considered a low rate.

23 MR. LIFLAND: Thank you.

24 MS. CONROY: Are you all

1 set? I just have a quick  
2 question.

3 THE VIDEOGRAPHER: Off the  
4 record, right?

5 MS. CONROY: Keep it on the  
6 record.

7 THE VIDEOGRAPHER: No  
8 problem.

9 - - -

10 EXAMINATION

11 - - -

12 BY MS. CONROY:

13 Q. Doctor, Exhibit 29 I'm going  
14 to ask you about. 29 is --

15 MR. LIFLAND: I've got it.  
16 It's the --

17 MS. CONROY: It is the risk  
18 management report plan, June 14,  
19 2007.

20 BY MS. CONROY:

21 Q. You just had it a minute  
22 ago. It's thick.

23 A. There are lots of documents.  
24 If it's this --

1 MR. LIFLAND: This one.

2 THE WITNESS: Okay. Okay.

3 Thank you.

4 BY MS. CONROY:

5 Q. And could you go to Page 39,  
6 please.

7 A. Yes.

8 Q. And I think earlier we were  
9 talking about the context in which  
10 certain words are used or you have to be  
11 careful of the context of a document. Is  
12 that true?

13 A. Yes.

14 Q. And if you take a look, I  
15 know that Mr. Lifland read to you that --  
16 he read the sentence, "For example, in a  
17 retrospective review of over 12,000  
18 hospital patients, only four potential  
19 addicts were identified." And that cites  
20 the Porter and Jick letter to the editor  
21 from 17 -- 27 years earlier.

22 But if you look at -- above  
23 that, it says, "One of the main  
24 misconception leading to the

1     undertreatment of pain by clinicians in  
2     the United States is exaggerated fear  
3     that efforts to adequately relieve pain  
4     will result in the development of  
5     addiction to the pain-relieving medicine.  
6     Clinicians commonly overestimate the  
7     frequency of addiction in hospitalized  
8     patients."

9                     And then it goes onto cite  
10    Porter and Jick. And says the survey  
11    data suggest low rates of iatrogenic  
12    addiction.

13                    Do you see that?

14                    A.     I do.

15                    Q.     So the context of this is  
16    that there are misconceptions with  
17    respect to concerns about iatrogenic  
18    addiction, and that it is in fact a low  
19    rate, correct?

20                    MR. LIFLAND: Object to the  
21    form of the question.

22                    THE WITNESS: In the context  
23    of stating that there are no large  
24    prospective studies that would get

1 to the exact rate, these are the  
2 best data that we have available.

3 BY MS. CONROY:

4 Q. And from that, you can -- if  
5 you're reading this, it's telling you  
6 there's a -- there's a misconception  
7 leading to the undertreatment of pain  
8 because people are more worried than they  
9 should be about iatrogenic addiction?

10 MR. LIFLAND: Object to the  
11 form of the question.

12 THE WITNESS: This is in the  
13 context of a report we're making  
14 to the Food and Drug  
15 Administration describing the --  
16 our risk management plan, but we  
17 make those statements.

18 BY MS. CONROY:

19 Q. Right. You make statements  
20 of misconception of undertreatment of  
21 pain to the FDA, and not statements about  
22 the lack of studies with respect to  
23 iatrogenic addiction?

24 MR. LIFLAND: Object to the

1 form of the question.

2 THE WITNESS: I'm not sure  
3 of the question. We did cite the  
4 Porter and Jick letter.

5 BY MS. CONROY:

6 Q. With a statement about the  
7 fact that there were misconceptions about  
8 concerns about addiction.

9 A. Yes.

10 Q. It would seem to -- it would  
11 seem to be contradictory.

12 MR. LIFLAND: Object to the  
13 form of the question.

14 THE WITNESS: It was -- I  
15 don't know that I'd call it  
16 contradictory. But that there are  
17 inadequate data. But that there  
18 was the general conception at the  
19 time, certainly information that  
20 we gathered even at advisory  
21 committees with the FDA, that  
22 the -- the concern about the  
23 potential for addiction led to  
24 undertreatment of pain.

1                   That was a widely cited  
2                   concern, even by the FDA at their  
3                   advisory committee meetings, there  
4                   were some data that assessed rates  
5                   of addiction, one of which was the  
6                   Porter & Jick letter.

7       BY MS. CONROY:

8               Q.       And so those concerns were  
9               stated by Janssen here without the  
10              benefit of any large scale addiction  
11              study?

12             A.       As we stated.

13                   MS. CONROY: That's all I  
14                   have.

15                   MR. LIFLAND: Just one quick  
16                   question. I'll do it from here.

17                   THE VIDEOGRAPHER: Your  
18                   microphone.

19                               -   -   -

20                               EXAMINATION

21                               -   -   -

22       BY MR. LIFLAND:

23               Q.       Can you read the sentence  
24               that begins "Clinicians commonly

1 overestimate"?

2 A. "Clinicians commonly  
3 overestimate the frequency of addiction  
4 in hospitalized patients."

5 Q. What patients is that  
6 sentence talking about?

7 A. I'd have to go to the  
8 reference. Well, that -- it's talking  
9 about hospitalized patients by virtue of  
10 the sentence.

11 Q. And what -- that's what it  
12 says. And what patients did the Porter &  
13 Jick survey look at?

14 A. Hospitalized patients.

15 Q. So in fact, the sentence is  
16 responding to a sentence about  
17 overestimation of addiction in  
18 hospitalized patients, correct?

19 A. Correct. In that respect  
20 we're looking at a similar patient  
21 population.

22 Q. And then can you read the  
23 final sentence of that paragraph?

24 A. "It should be noted that

1     there have been no large prospective  
2     studies of iatrogenic drug addiction, but  
3     these survey data suggest low rates of  
4     iatrogenic addiction."

5             Q.     So the absence of large  
6     scale prospective studies is expressly  
7     noted, right?

8             A.     Yes.

9             MR. LIFLAND:   Thank you.

10                     -   -   -

11                     EXAMINATION

12                     -   -   -

13     BY MS. CONROY:

14             Q.     Just take a look.   Prior to  
15     the sentence about the "clinicians  
16     commonly overestimate the frequency of  
17     addiction in hospitalized patients,"  
18     there's no definer of the types of  
19     clinicians in the sentence above.   One of  
20     the main misconceptions leading to  
21     undertreatment of pain by clinicians in  
22     the United States is exaggerated fears  
23     that efforts to adequately relieve pain  
24     will result in the development of

1 addiction to pain relieving medicine.

2 That has no qualifier with  
3 respect to hospitals or hospital  
4 patients, correct?

5 A. Correct.

6 MS. CONROY: No further  
7 questions.

8 THE VIDEOGRAPHER: This  
9 marks the end of today's  
10 deposition. The time is 8:01 p.m.  
11 We are off the record.

12 (Brief pause.)

13 - - -

14 MS. CONROY: As a  
15 housekeeping detail to the  
16 30(b)(6) deposition, I know that I  
17 marked as exhibits all of the  
18 index sheets to the documents that  
19 were provided to us by defense  
20 counsel, and we did not mark  
21 separately all of the documents,  
22 we just marked the index sheets.  
23 And so at this time, we will  
24 mark -- we won't do it here at the

1 deposition, but we will consider  
2 that all of the documents  
3 referenced on the index sheets are  
4 part of the exhibit, and we can  
5 label them, the exhibit number A,  
6 if you want or we can --

7 MR. LIFLAND: Should we do  
8 it that way? I'm fine with that.

9 And for the record, I just  
10 have an objection here. There  
11 were three exhibits, I guess one  
12 was simply his --

13 MS. CONROY: That one is  
14 marked as an exhibit.

15 MR. LIFLAND: I'd like to  
16 have them all here. There was  
17 another one yesterday, right?

18 MS. CONROY: I think he has  
19 that one. Here is the other one.

20 MR. LIFLAND: There was  
21 another one yesterday.

22 MS. CONROY: There was. Let  
23 me -- I'll tell you what, I will  
24 find that and I will mark it as

1           Exhibit 43 and we'll put it in the  
2           record.   Okay?

3                   (Document marked for  
4           identification as Exhibit  
5           Janssen-Moskovitz-42.)

6                   (Document marked for  
7           identification as Exhibit  
8           Janssen-Moskovitz-43.)

9                   MR. LIFLAND:   Just for the  
10          record, these are pictures of the  
11          witness in which counsel has  
12          written excerpts from documents.  
13          I believe these are not proper  
14          argument.   They shouldn't have  
15          been displayed while the testimony  
16          was being taken, and I would  
17          object to them being displayed  
18          with the testimony, if the  
19          testimony is played.   So I just  
20          want to make that objection for  
21          the record.

22                   I appreciate having a copy  
23          of these, you know, for our  
24          purposes.

1 MS. CONROY: Sure. And we  
2 consider these demonstratives that  
3 would takes place at this  
4 deposition. If used as trial they  
5 would be perfectly possible to  
6 create during trial and so we may  
7 have -- we may have additional  
8 justification if it comes -- if it  
9 ever comes to that. But that's  
10 our position right now.

11 MR. LIFLAND: Okay.

12 (Excused.)

13 (Deposition concluded at  
14 approximately 8:05 p.m.)  
15  
16  
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18  
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1  
2 CERTIFICATE  
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4

5 I HEREBY CERTIFY that the  
6 witness was duly sworn by me and that the  
7 deposition is a true record of the  
8 testimony given by the witness.

9 It was requested before  
10 completion of the deposition that the  
11 witness, BRUCE L. MOSKOVITZ, M.D., have  
12 the opportunity to read and sign the  
13 deposition transcript.

14  
15 \_\_\_\_\_  
16 MICHELLE L. GRAY,  
17 A Registered Professional  
18 Reporter, Certified Shorthand  
19 Reporter, Certified Realtime  
20 Reporter and Notary Public  
21 Dated: November 15, 2018  
22  
23  
24

25 (The foregoing certification  
26 of this transcript does not apply to any  
27 reproduction of the same by any means,  
28 unless under the direct control and/or  
29 supervision of the certifying reporter.)  
30  
31  
32

1 INSTRUCTIONS TO WITNESS

2  
3 Please read your deposition  
4 over carefully and make any necessary  
5 corrections. You should state the reason  
6 in the appropriate space on the errata  
7 sheet for any corrections that are made.

8 After doing so, please sign  
9 the errata sheet and date it.

10 You are signing same subject  
11 to the changes you have noted on the  
12 errata sheet, which will be attached to  
13 your deposition.

14 It is imperative that you  
15 return the original errata sheet to the  
16 deposing attorney within thirty (30) days  
17 of receipt of the deposition transcript  
18 by you. If you fail to do so, the  
19 deposition transcript may be deemed to be  
20 accurate and may be used in court.

1

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E R R A T A

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4 PAGE LINE CHANGE

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1  
2 ACKNOWLEDGMENT OF DEPONENT

3  
4 I, \_\_\_\_\_, do  
5 hereby certify that I have read the  
6 foregoing pages, 326 - 769, and that the  
7 same is a correct transcription of the  
8 answers given by me to the questions  
9 therein propounded, except for the  
10 corrections or changes in form or  
11 substance, if any, noted in the attached  
12 Errata Sheet.

13  
14  
15 \_\_\_\_\_  
16 BRUCE L. MOSKOVITZ, M.D.

DATE

17  
18  
19 Subscribed and sworn  
to before me this

20 \_\_\_\_\_ day of \_\_\_\_\_, 20\_\_\_\_.

21 My commission expires: \_\_\_\_\_

22  
23 \_\_\_\_\_  
Notary Public

Highly Confidential - Subject to Further Confidentiality Review

	LAWYER'S NOTES		
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